multiplied by 100 to give the percent deuterium incorporation for each position.

(b) Hydrogen–Deuterium Exchange of Levulinaldehyde (2). (i) Dabco plus Acetic Acid-*d* and Dabco plus 2-Propanol-*d*. Two solutions (1.0 mL) were prepared volumetrically from freshly sublimed Dabco (2.0 mg, 0.018 mmol), 4-deuterio-1-methoxybenzene (**26**) (100 μL, 99.5 mg, 0.92 mmol), and pure[34b] levulinaldehyde (**2**) (59 mg, 0.59 mmol) in CCl_4 and in dry C_6H_6. Two aliquots (0.4 mL) of each solution were placed into four 5-mm NMR tubes. Acetic acid-*d* (70 μL, 73 mg, 1.2 mmol) was added to two of the aliquots, one in CCl_4 and the other in C_6H_6, and 2-propanol-*d* (16 μL, 13 mg, 0.20 mmol) was added to the two remaining aliquots.

The concentration of levulinaldehyde (**2**) relative to the internal standard **26** was determined by ^1H NMR (60 MHz) spectroscopy using the ratios of integrated areas of the peaks at δ 9.72 (s, 1 H) (CCl_4) and 9.38 (s, 1 H) (C_6H_6) and 3.74 (s, 3 H) (CCl_4) and 3.46 (s, 3 H) (C_6H_6) for **2** and **26** (0.92 M), respectively. Next, the amount of deuterium incorporation in **2** was determined relative to the internal standard **26** by ^2H NMR (15.36 MHz) spectroscopy. The ratios of the integrated areas of the ^1H-decoupled ^2H NMR signals at δ 2.72 (s, 1 ^2H) (CCl_4) and 3.18 (s, 1 ^2H) (C_6H_6) and 2.18 (s, 1 ^2H) (CCl_4) and 2.68 (s, 1 ^2H) (C_6H_6), which corresponded to signals for the methylene resonances of deuterated **2**, and δ 6.96 (s, 1 ^2H) (CCl_4) and 7.80 (s, 1 ^2H) (C_6H_6), which corresponded signals for the internal standard **26**, were used to calculate the amount of deuterium incorporated in **2**.[51]

The four NMR tubes were allowed to stand at room temperature for 60 h.[52] ^1H NMR (60 MHz) and ^2H NMR (15.36 MHz) were recorded periodically and the amount of deuterium incorporated in the methylene and methyl positions of **2** was determined and these values were divided by the concentration of **2** (which was determined from the aldehydic protium resonance) and multiplied by 100 to give the percent deuterium incorporation in each position.

(ii) Me_4NOAc plus Acetic Acid-*d* and Me_4NOAc plus 2-Propanol-*d*. A solution (0.42 mL) was prepared volumetrically in a 5-mm NMR tube containing 4-deuterio-1-methoxybenzene (**26**) (15 μL, 15 mg, 0.14 mmol, 0.33 M), acetic acid-*d* (2.8 μL, 2.9 mg, 0.048 mmol), and a 0.012 M Me_4NOAc in dry $CHCl_3$ solution. The concentration of acetic acid-*d* relative to Me_4NOAc was determined by ^1H NMR spectroscopy. The procedure for preparing the 0.012 M Me_4NOAc in $CHCl_3$ solution and the method for calculating the concentration of acetic acid-d_1 relative to Me_4NOAc is described above under "Preparation of Catalyst Solutions". A second solution (0.42 mL) was prepared volumetrically in a 5-mm NMR tube containing 4-deuterio-1-methoxybenzene (**26**) (15 μL, 15 mg, 0.14 mmol, 0.33 M), 2-propanol-*d* (19 μL, 15 mg, 0.25 mmol, 0.59 M), and a 0.012 M Me_4NOAc in dry $CHCl_3$. Both solutions were combined with levulinaldehyde (**2**) (25 mg, 0.25 mmol, 0.59 M) and mixed thoroughly by shaking. The concentration of levulinaldehyde (**2**) relative to the internal standard **26** was determined by ^1H NMR (60 MHz) spectroscopy using the ratios of integrated areas of the peaks at δ 9.77 (s, 1 H) and 3.53 (s, 3 H) for **2** and **26** (0.33 M), respectively. Next the amount of deuterium incorporation in **2** was determined relative to the internal standard **26** by ^2H NMR (15.36 MHz) spectroscopy. The ratios of the integrated areas of the ^1H decoupled ^2H NMR signals at δ 2.79 (s, 1 ^2H) and 2.21 (s, 1 ^2H), which correspond to signals for the methylene and methyl resonances of deuterated **2** and δ 7.02 (s, 1 ^2H) for **26** were used to calculate the amount of deuterium incorporated in **2**.

The two solutions were heated at 37 °C in a thermostated oil bath at 37 °C for 60 h.[51] ^1H NMR (60 MHz) and ^2H NMR (15.36 MHz) were recorded periodically, the concentrations of deuterium incorporated in the methylene and methyl positions of **2** were determined, and these values were divided by the concentration of **2** (which was determined from the aldehydic protium resonance) and multiplied by 100 to give the percent deuterium incorporation in each position.

Acknowledgment. We thank Professor P. M. McCurry, Jr. for helpful suggestions and the National Institutes of Health for financial support of this research through Grant GM-21249 from the Division of General Medical Sciences.

(51) As the amount of deuterium increased in methylene positions of **2** as measured by ^2H NMR, a corresponding decrease in the integral height of the methylene ^1H NMR resonance at δ 2.26 (C_6H_6) or 2.54 (CCl_4) occurred.

(52) Control experiments have shown that levulinaldehyde is stable to Dabco or Me_4NOAc plus acetic acid and neat acetic acid, even after prolonged heating at 45 °C.[1] In contrast, 3-hydroxycyclopentanone (**6**) is slowly and quantitatively converted to cyclopent-2-en-1-one (**7**) under these conditions.

Ring Expansion and Cleavage of Succinoin Derivatives. Geminal Acylation, Reductive Succinoylation, and Stereoselective Spiro Annelation Methods

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Contribution from the Department of Chemistry, Tokyo Institute of Technology, Meguro, Tokyo 152, Japan. *Received April 21, 1983*

Abstract: The Lewis acid catalyzed aldol-type reaction of 1,2-bis(trimethylsiloxy)cyclobutene and a ketal or an acetal gives a succinoin derivative. This cyclobutanone undergoes several types of acid-catalyzed transformations either as it is or after alkylidenation or reduction of the carbonyl group. The reactions provide useful synthetic entries to various compounds such as 1,3-cyclopentanediones, 4-keto acids and esters, 3-alkylidenecyclopentan-1-ones, and 2- and 3-cyclopenten-1-ones. The stereochemistry of the initial aldol reaction and some of these acid catalyzed reactions have been examined to find a new and reliable approach to the stereoselective construction of (spiro) quaternary centers. Formal syntheses of two sesquiterpenes, *dl*-cuparene and *dl*-lanceol, are also described.

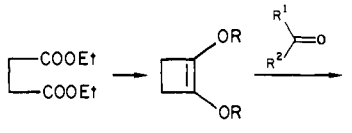
The use of chlorotrimethylsilane in acyloin condensation has immensely multiplied the value of this long-known reaction.[1] The effect of the added chlorosilane is particularly dramatic in the reductive cyclization of dialkyl succinates (eq 1), with which the conventional conditions failed to give the cyclized products.[2]

In relation to our interests in the reaction of enol silyl ethers and carbonyl compounds, we became intrigued by the aldol chemistry of **1** as well as the synthetic potential of the resultant aldol adduct **2a** as a precursor of cyclopentanones, inter, alia,

†UNESCO Fellow 1980–1981.

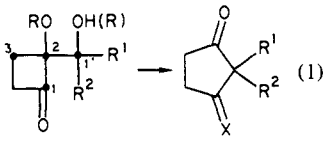
(1) (a) Reviews: Ruhlmann, K. *Synthesis*, **1971**, 236. (b) Bloomfield, J. J.; Owsley, D. C.; Nelke, J. M. *Org. React. (N.Y.)* **1976**, *23*, 259.
(2) Bloomfield, J. J.; Nelke, J. M. *Org. Synth.* **1977**, *58*, 1.

0002-7863/84/1506-1759$01.50/0



1

R = $SiMe_3$

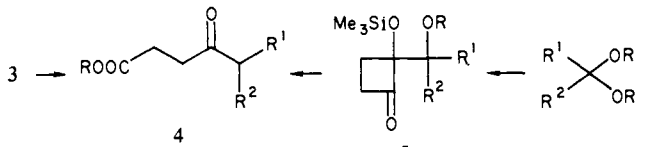


2a: X = O
b: X = CH_2
c: X = $OSiMe_3$

3a,b,c

1,3-cyclopentanediones **3a**[3] (eq 1). Attached directly to the diol moiety, the cyclobutanone ring would be expected to exert directive effects in the cationic rearrangement of **2a**. Since the transformation from a carbonyl compound (aldehydes, acetals, or ketals) to diketone **3a** represents the net replacement of the C=O double bond by two geminally substituted acyl groups, we have termed it geminal acylation.[4] The utility of 1,3-cyclopentanediones has already been established in steroid and other natural product synthesis.[3] The present method is particularly interesting as an approach to spiro ring systems.[5]

Diketone **3a** is subject to base-catalyzed ring cleavage; γ-keto acid **4** therefore becomes available from a carbonyl compound,



4 5

(2)

and the attachment of the succinoyl group in a reductive manner (reductive succinoylation) is readily achieved.[6,7] A useful ancillary was the unexpectedly facile ring cleavage of **5**, which provided an additional and more efficient method for the preparation of γ-keto esters.

Conversion like that of **2** to **3** would be a potentially useful method for the stereoselective construction of quaternary centers (1) if the initial aldol reaction is stereoselective and/or (2) if we can find a stereoselective process that eventually produces a chiral center in **3**. Though the method in its original symmetrical situation (eq 1, series **a**) does not allow the investigation of such problems, we were gratified to find that the desirable property is already installed in the initial aldol process (**1** to **2**) and that the use of methylene (series **b**) and siloxycyclobutanes (series **c**) derivatives results in the stereoselective formation of quaternary centers (**3b** and **3c**).[8]

Results and Discussion

Geminal Acylation Route to 1,3-Cyclopentanediones. Several types of methods are available to effect the aldol reaction[9] between the cyclobutene **1** and carbonyl compounds. It soon became apparent, however, that Lewis acid catalyzed conditions[10] serve

(3) 1,3-Cyclopentanedione use in steroid synthesis: Blickenstaff, R. T.; Ghosh, A. C.; Woff, G. C. "Total Synthesis of Steroids"; Academic Press: New York, 1974. Preparation: Hengartner, U.; Chu, U. *Org. Synth.* **1978**, *58*, 83, and referenced therein.
(4) Preliminary report: Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 961.
(5) Review: Krapcho, A. P. *Synthesis*, **1976**, 425. Martin, S. F. *Tetrahedron*, **1980**, *36*, 419.
(6) Preliminary report: Nakamura, E.; Hashimoto, K.; Kuwajima, I. *J. Org. Chem.* **1977**, *42*, 4166.
(7) Recent approach to reductive succinoylation: Trost, B. M.; Gowland, F. W. *J. Org. Chem.* **1979**, *44*, 3448.
(8) Part of the results have been presented orally at the 4th ICOS meeting in Tokyo, 1982: Kuwajima, I.; "IUPAC Current Trends in Organic Synthesis"; Nozaki, H., Ed.; Pergamon Press: Oxford, 1983; pp 311–322.
(9) Mukaiyama, T. *Org. Synth.* **1982**, *28*, 203.

Table I. Preparation of Succinoin Derivatives (See Chart I)

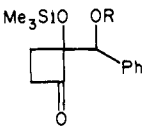
adduct	% yield	adduct	% yield	adduct	% yield
6	78	12	76	18	90
7	75	13	90	19	70
8	94	14	89	20	92
9	91	15	90	21	87
10	87	16	92	22	60
11	100	17	90		

Table II. Preparation of Diketones 23–31 (See Chart II)

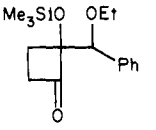
succinoins	diketones	% yield
7	23	97
8	23	93
14	24	78
15	25	87
16	26	87
18	27	88
20	28	94 (91)[a]
21	29, 30	69, 26
22	31	92

[a] Overall yield from the ketal without isolating the succinoin 20.

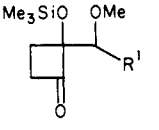
Chart I



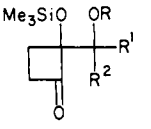
6: R = H
7: R = $SiMe_3$



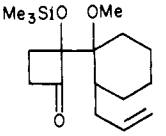
8



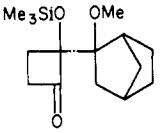
9: R^1 = Ph
10: R^1 = *p*-ClC_6H_4
11: R^1 = *p*-$CH_3C_6H_4$
12: R^1 = PhCH=CH
13: R^1 = *n*-PrCH=CH
14: R^1 = *n*-C_5H_{11}
15: R^1 = *n*-C_9H_{19}



16: R = CH_3, R^1 = R^2 = C_2H_5
17: R = CH_3, R^1,R^2 = $(CH_2)_5$
18: R = C_2H_5, R^1,R^2 = $(CH_2)_5$
19: R = CH_3, R^1,R^2 = $(CH_2)_7$
20: R = CH_3, R^1,R^2 = $(CH_2)_{11}$

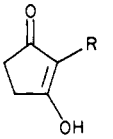


21

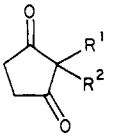


22

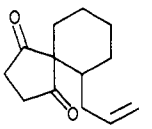
Chart II



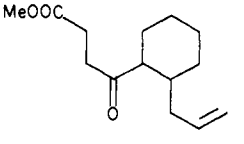
23: R = C_6H_5
24: R = *n*-C_5H_{11}
25: R = *n*-C_9H_{19}



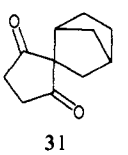
26: R^1 = R^2 = C_2H_5
27: R^1,R^2 = $(CH_2)_5$
28: R^1,R^2 = $(CH_2)_{11}$



29

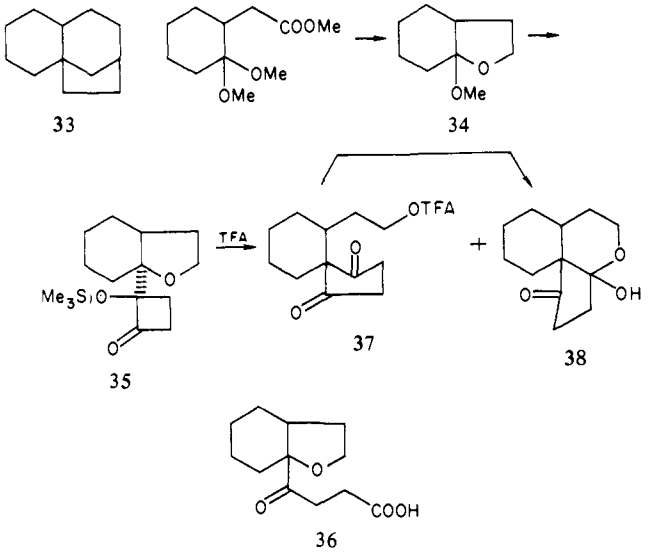


30



31

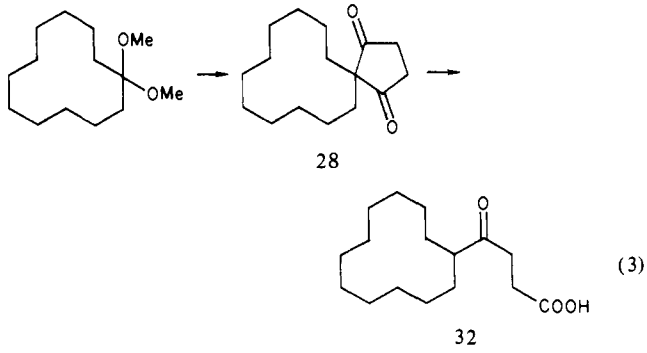
Scheme I



best for this purpose. $TiCl_4$ gave the most satisfactory results for the reaction with aldehydes and aliphatic acetals, but less vigorous $BF_3{\cdot}Et_2O$ was the reagent of choice for the more reactive acetals and ketals. The aldol reaction between **1** and ketones could not be achieved under a variety of acidic or basic conditions.[11,12] The results of the aldol coupling are summarized in Table I.

The transformation of the aldol product to the diketone **3a** was effected smoothly by excess trifluoroacetic acid (TFA) (Table II). Our choice of TFA depended mainly on the ease of removal of the solvent upon workup. *p*-Toluenesulfonic acid in hot benzene, $BF_3{\cdot}Et_2O$, and trimethylsilyl triflate (TMSOTf) in methylene chloride were also effective. The reaction of the four aldol adducts, **7**, **8**, **15**, and **18**, were examined by ^1H NMR at 35 °C with 40 equiv of TFA as solvent. The reaction rate was highly dependent on the substrate. The ketal adduct reacted most rapidly, while the adduct derived from an aliphatic acetal showed very slow conversion; half-lives of ca. 71 h, 1 h, 1 h, and less than a few minutes were recorded for **15**, **7**, **8**, and **1**,, respectively. The rearrangement of the adduct formed from unsaturated acetals, e.g., **12** and **13**, gave complex results.

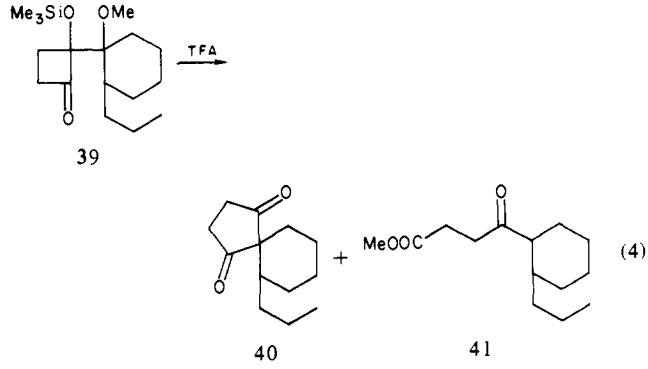
The diketone can readily be converted to the γ-keto acid under basic conditions.[13] Treatment of **28** with sodium hydroxide in hot methanol produced **32** in 62% yield; the reductive succinoylation sequence provides a simple entry to this useful class of compounds.[14]



(3)

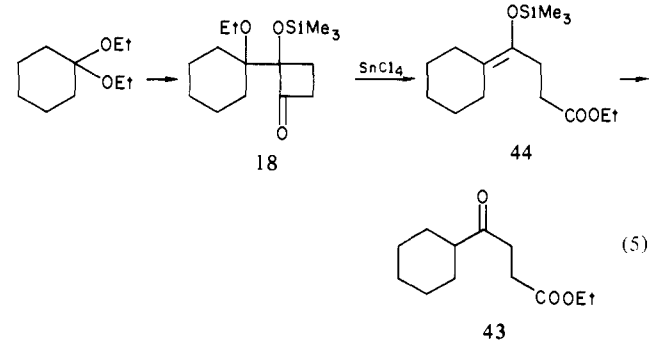
As a prospective approach to a tricyclic skelton **33** commonly seen among diterpenes,[15] the reaction of the ketal **34** was examined (Scheme I). The reaction of **34** with **1** gave **35** as a mixture of two diastereomers, which gave **36** as a single isomer upon oxidative cleavage of the cyclobutanone ring.[16] The stereochemistry of **35** is expected to be as indicated (vide infra). Treatment of **35** with TFA followed by K_2CO_3/methanol treatment (to convert **37** to **38**) gave **38** in 70% yield. Conversion of **38** to **33** is the subject of further study.

A related substrate, **29**, prepared from 2-allylcyclohexanone ketal, was subjected to the TFA-catalyzed rearrangement (Table II, entry 8). Surprisingly, a substantial amount of keto ester **30** formed along with the desired diketone **27** (69%) under a variety of conditions. Similarly, the substrate with a propyl side chain (**39**) also gave a diketone (**40**) (70%) and keto ester (**41**) (26%) mixture (eq 4).



(4)

Reductive Succinoylation of Ketone Functionality. During the foregoing studies, we encountered several instances in which the cyclobutanone ring was cleaved under acidic conditions to form γ-keto esters. Intrigued by the possibility of developing a single-step synthesis of γ-keto esters by the reductive succinoylation method, we studied the optimization of this ring-cleavage reaction. Initial experiments involved the treatment of cyclobutanone **18** with a stoichiometric amount of acids. $BF_3{\cdot}Et_2O$ and TMSOTf gave **27** as the only product; however, $SnCl_4$, $AlCl_3$, $TiCl_4$, and $SbCl_5$ converted **17** solely into the ring cleavage product. It soon became apparent that the formation and the ring opening of **18** could be accomplished in a single operation with $SnCl_4$. Addition of a mixture of **1** and the ketal to a solution of $SnCl_4$ gave the desired product **43** in 93% yield. The enol silyl ether **44**, the initial product of the reaction, could also be isolated from the workup if it were quenched with a tertiary amine[17] before aqueous treatment (eq 5).

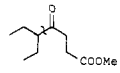
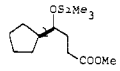
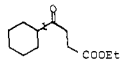
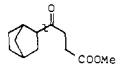
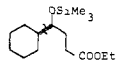
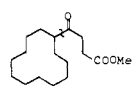
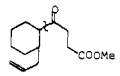
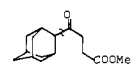
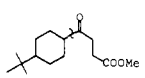
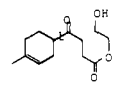
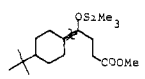
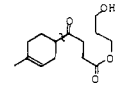


(5)

For further optimization, diverse conditions were tried for some common substrates; it was found that the ease of the ring cleavage markedly depends on the structure of the substrate. For instance, the aldol adducts derived from the cyclohexanone and cyclopentanone ketals rearrange smoothly in the presence of a small

(10) Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503.
(11) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4464.
(12) Nakamura, E.; Shimizu, M.; Kuwajima, I.; Sakata, J.; Yokoyama, K.; Noyori, R. *J. Org. Chem.* **1983**, *48*, 932.
(13) Cf.: House, H. O. "Modern Synthetic Reactions"; Benjamin: Menlo Park, CA, 1972; p 760.
(14) Cf.: (a) Shono, T.; Nishiguchi, I.; Ohmizu, H. *J. Am. Chem. Soc.*, **1977**, *99*, 7396. (b) Wehri, P. A.; Chu, V. *J. Org. Chem.* **1973**, *38*, 3437; *Org. Synth.* **1978**, *58*, 81.
(15) Nakanishi, K.; Goto, T.; Ito, S.; Natori, S.; Nozoe, S. "Natural Product Chemistry"; Kodansha: Tokyo, 1974; Vol. 1, Chapter 4.
(16) Trost, B. M.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 5321.
(17) Cf.: Denis, J. M.; Girard, C.; Conia, J. M. *Synthesis* **1972**, 549.

Table III. Reductive Succinoylation Method

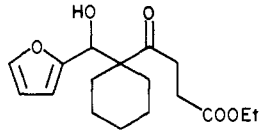
ketoesters	compd no.	% yield	ketoesters	No.	% yield
	42	87		47	89[a]
	43	93		48	90
	44	85[a]		49	91
	30	70		50	68
	45	92		51	46
	46	93[a]		52	54

[a] Triethylamine quench (see Experimental Section).

of amount of the catalyst, while the acetone adduct proved quite stable and ring enlargement to the diketone also occurred under forcing conditions. The tricyclic adduct **35** also behaved similarly. Adducts formed from acetals are inert to $SnCl_4$. The results of the reductive succinoylation procedure are summarized in Table III.

The 1,4-disposition of the carbonyl groups in the γ-keto ester suggests the conversion to 1,5-diene systems. Application of this concept led to a synthesis of *dl*-lanceol (**56**) (Scheme II). Unlike the dialkyl ketals studied above, the reaction of the ethylene ketal of 4-methyl-3-cyclohexen-1-one examined initially posed considerable problems, but finally the keto ester **52** was obtained in 54% isolated yield (from the ketal). Methylenation of acid **53** by the Nozaki method[19] gave **54** in 66% yield after esterification. The alcohol **55** obtained by hydride reduction has previously been converted to *dl*-lanceol.[18]

The enol silyl ether of the γ-keto ester, e.g., **44**, finds synthetic use. For instance, **44** reacts with furfural in the presence of tetrabutylammonium fluoride to give aldol **57**.[12] The enol silyl ether prepared in situ can be used for certain synthetic operations; quenching the reaction mixture containing **44** with phenylsulfenyl chloride[20] gave **58** in 78% yield (from the ketal). More significantly, the coupling of three components, **1**, 2-methylcyclohexanone dimethyl ketal, and benzaldehyde dimethyl acetal, was achieved in 70% yield (to obtain **59**) by sequential addition of these reactants to $SnCl_4$ at low temperatures.



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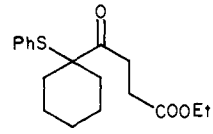

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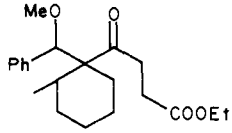
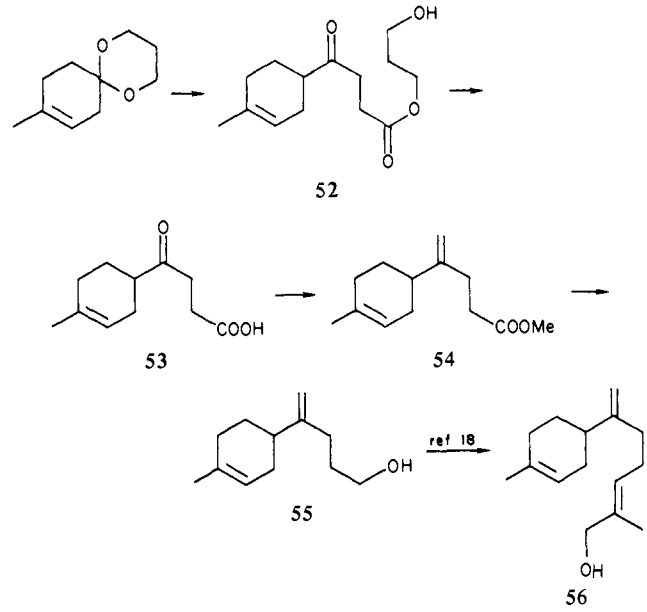


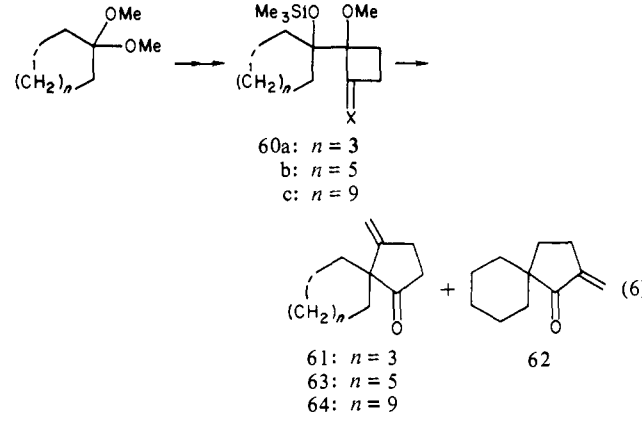
59

Scheme II



Stereoselective Spiro Annelation Method. With completion of the preceding work, we contemplated the stereochemical course of the reaction. Though the prochiral nature of the 1,3-diketone **3a** is often a desirable feature for synthesis,[3] this in turn makes the stereochemistry of the preceding reactions obscure. We therefore took two systems for stereochemical examination, one with methylenecyclobutane **2b**, which would conform to a well-founded protocol of neighboring group participation,[21] and the other with siloxybutane **2c**, which would most likely rearrange in a stepwise manner.[22] An additional interest in the methylenecyclobutane case is the expected production of 3-methylenecyclopentan-1-ones (**3b**), since this suggests the possible elaboration of this synthesis into intermediates for steroid[23] and trichothecane synthesis.[24]

The initial studies were made on the conversion of cyclohexanone dimethyl ketal to spiro[4.5]decane **61** (eq 6). The



60a: $n = 3$
b: $n = 5$
c: $n = 9$

61: $n = 3$
63: $n = 5$
64: $n = 9$

62

(6)

Wittig methylenation of **16** at first posed an unexpected problem, yet the ylide generated from $Ph_3CH_3P^+Br^-$ or BF_4^- and KH in THF was found to work very well. The results of extensive experimentation indicated that "salt-free"[25] conditions are essential for the olefination of this sterically congested cyclobutanone. Conditions involving the use of the sodium salt of dimethyl sul-

(18) Crawford, R. J.; Erman, W. F.; Broaddus, C. D. *J. Am. Chem. Soc.* **1972**, *94*, 4298.
(19) Takai, T.; Hotta, Y.; Oshima, K.; Nozaki, *Tetrahedron Lett.* **1978**, 2417.
(20) Murai, S.; Kuroki, Y.; Hasegawa, K.; Tsutsumi *J. Chem. Soc., Chem. Commun.* **1972**, 946.
(21) le Noble, W. J. "Highlights of Organic Chemistry"; Marcel Dekker: New York, 1974; p 700.
(22) Kuwajima, I.; Azegami, I. *Tetrahedron Lett.* **1979**, 2369.
(23) Cf.: Kametani, T.; Nemoto, H. *Tetrahedron* **1981**, *37*, 3.
(24) Cf.: Schlessinger , R. H.; Nugent, R. A. *J. Am. Chem. Soc.* **1982**, *104*, 1116.
(25) (a) Cf.: Schlosser, M. *Top. Stereochem.* **1970**, *5*, 1. (b) Trost, B. M.; Latimer, L. H. *J. Org. Chem.* **1978**, *43*, 1031.

Table IV. Effect of the Catalyst on the Rearrangement of 60a

entry	catalyst, (equiv)	solvent	condtns, °C, min	% yield[a] 61	62
1	TFA (5)	CH_2Cl_2	0-20, 20	74	(4)
2	TFA (5)	C_6H_6	0-20, 30	(67)	nd[b]
3	TFA (5)	CF_3CH_2OH	0-20, 35	81	nd[b]
4	aq. HBF_4 (5M)	$THF:H_2O$ (1:1)	20, 30 h	(68)	nd[b]
5	TfOH (0.1)	CF_3CH_2OH	0-20, 70	(81)	nd[b]
6	BF_3·Et_2O (1)	$CDCl_3$	0-20, 60	53	29
7	$SnCl_4$ (1)	$CDCl_3$	0-20, 15	(68)	nd[b]
8	$SnCl_4$ (1)	CF_3CH_2OH	−40-0, 90	(58)	nd[b]
9	Me_3SiOTf (1)	$CDCl_3$	0, 15	(70)	(5)
10	Me_3SiOTf (1)	CF_3CH_2OH	−40-0, 90	(32)	nd[b]
11	Et_2AlCl (1)	$CDCl_3$	0-20, 13 h	nr[c]	
12	Et_2AlCl (1)	C_6H_6	0-20, 13 h	nr[d]	
13	*p*-TsOH	C_6H_6	reflux, 180	complex	

[a] Isolated yield; ^1H NMR yield with an internal standard in parentheses. [b] Not detected. [c] No reaction; 84% recovery of 60a. [d] No reaction; 77% recovery of 60a.

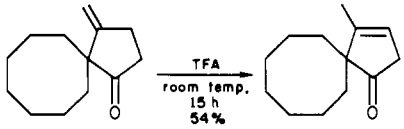
Table V. Spiro[4.*n*]alkane Synthesis

compd series	ketal	% yield aldol	Wittig	rearrnt
a	cyclohexanone dimethyl ketal	17, 90	60a, 92	61, 74
b	cyclooctanone dimethyl ketal	19, 70	60b, 90	63, 82
c	cyclododecanone dimethyl ketal	20, 92	60c, 67	64, 72

foxide or potassium *tert*-amylate tended to effect partial loss of the silyl group from the product.

The ring enlargement of **60a** to **61** could be effected by a number of protic or Lewis acids with widely varying yields (Table IV). TFA or trifluoromethanesulfonic acid (TfOH) in 2,2,2-trifluoroethanol turned out to be the best. Methylene chloride was often a good substitute for the more expensive trifluoroethanol. Although the TFA catalyzed rearrangement in trifluoroethanol gave **61** as a single product, the BF_3·Et_2O catalyzed reaction gave as much as 22% of the "wrong" isomer **62**. This side reaction was also detected in some other cases (Table IV). Cyclooctanone and cyclododecanone ketals reacted similarly to afford **63** and **64** via **60b** and **60c**, respectively (Table V).

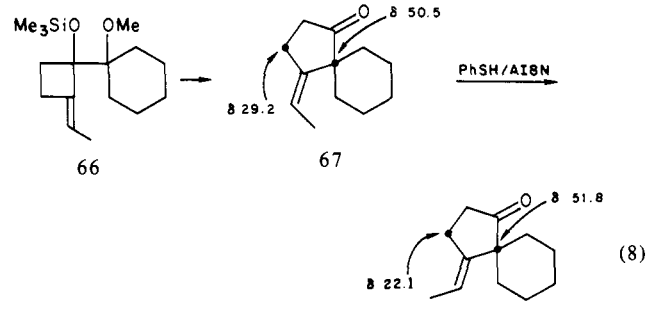
The 3-methylenecyclopentanones such as **63** readily isomerize to the more stable endo olefinic isomers such as **65** in good yield. None of the conjugated enones were formed in the reaction. These products were also obtained directly from **3b** by prolonged acidic treatment (eq 7).



63 65 (7)

We then examined the rearrangement of the ethylidenecyclobutanone **66** available in 69% yield from **16**; the stereochemistry of the ethylidene group is potentially subject to isomerization during the rearrangement. The Wittig reaction gave a 8:92 mixture of *E*/*Z* isomers, the assignment being made in analogy to the results with 2,2-dialkylcyclanones.[26] TFA treatment of **66** gave **67** in 66% yield as a 2:98 mixture of *E*/*Z* isomers. The rearrangement therefore proceeded with retention of the olefin geometry (eq 8).

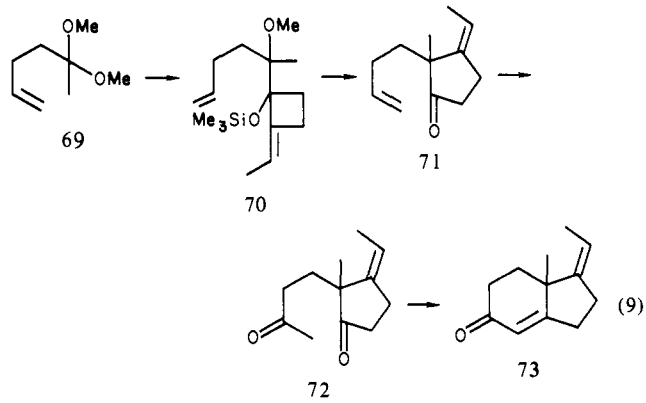
The *Z*-isomer **67** smoothly isomerizes to **68** (*E*:*Z* = 97:3) on treatment with PhSH/AIBN.[27] This clean conversion is the



66 67 68 (8)

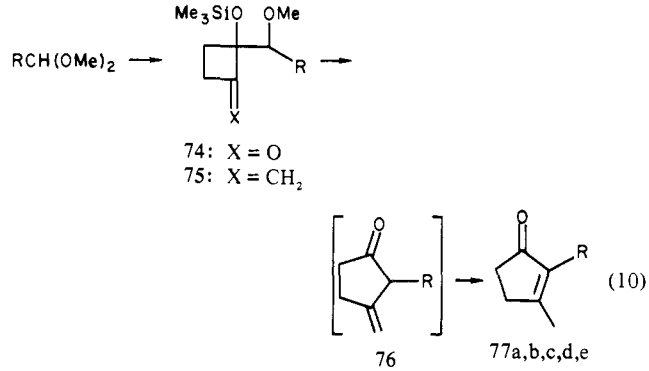
chemical proof of the *Z*-geometry of **67**. ^{13}C NMR spectra of **67** and **68** also supported the assigned geometry; the carbon atom on the same side of the olefinic methyl group suffers upfield shift due to steric compression[28] (eq 8).

The annelation sequence applies equally to aliphatic ketals. Following the standard steps, allylacetone ketal **69** was converted to **71** in 75% yield. The rearranged product **71** obtained in 46% overall yield was about 90% stereochemically pure. Ketone **71** is a synthetically interesting compound. For instance, selective oxidation of the monosubstituted olefin under Pd catalysis (**72**)[29] and internal aldolization gave hydrindanone **73** (eq 9).



69 70 71 72 73 (9)

The viability of the present scheme in annelating a ring on an acetal function was then examined (eq 10).[30] Coupling with **1**



74: X = O
75: X = CH_2

76 77a,b,c,d,e (10)

and the Wittig olefination proceeded without event. The attempted rearrangement of cyclobutane **75** (R = alkyl) gave an intractable product mixture. On the other hand, the compounds derived from

(26) Cf.: Batcho, A. D.; Berger, D. E.; Uskokovic, M. R.; Snider, B. B. *J. Am. Chem. Soc.* **1981**, *103*, 1293. Batcho, A. D.; Berger, D. E.; Davoust, S. G.; Wovkulich, P. M.; Uskokovic, M. R. *Helv. Chim. Acta* **1981**, *64*, 1682. Dauben, W. G.; Brookhart, T. *J. Am. Chem. Soc.* **1981**, *103*, 237.

(27) Sonnet, P. E. *Tetrahedron* **1980**, *36*, 557. Henrick, C. A.; Willy, W. E.; Baum, J. W.; Bear, T. A.; Garcia, B. A.; Maste, T. A.; Chang, S. M. *J. Org. Chem.* **1975**, *40*, 1. Bhalerav, U. T.; Rapoport, H. *J. Am. Chem. Soc.* **1971**, *93*, 4835.

(28) Wilson, N. K.; Stothers, J. B. *Top. Stereochem.* **1973**, *10*, 1. Lippman, E.; Pelk, T.; Paasiviria, J.; Belikova, N.; Plate, A. *Org. Magn. Reson.* **1970**, *2*, 581.

(29) Tsuji, J.; Shimizu, I.; Yamamoto, K. *Tetrahedron Lett.* **1976**, 2975: Tsuji, J.; Kobayashi, Y.; Kataoka, H.; Takahashi, T. *Ibid.* **1980**, *21*, 3393.

(30) Nakamura, E.; Shimada, J.; Kuwajima, I. *J. Chem. Soc., Chem. Commun.* **1983**, 499.

Scheme III

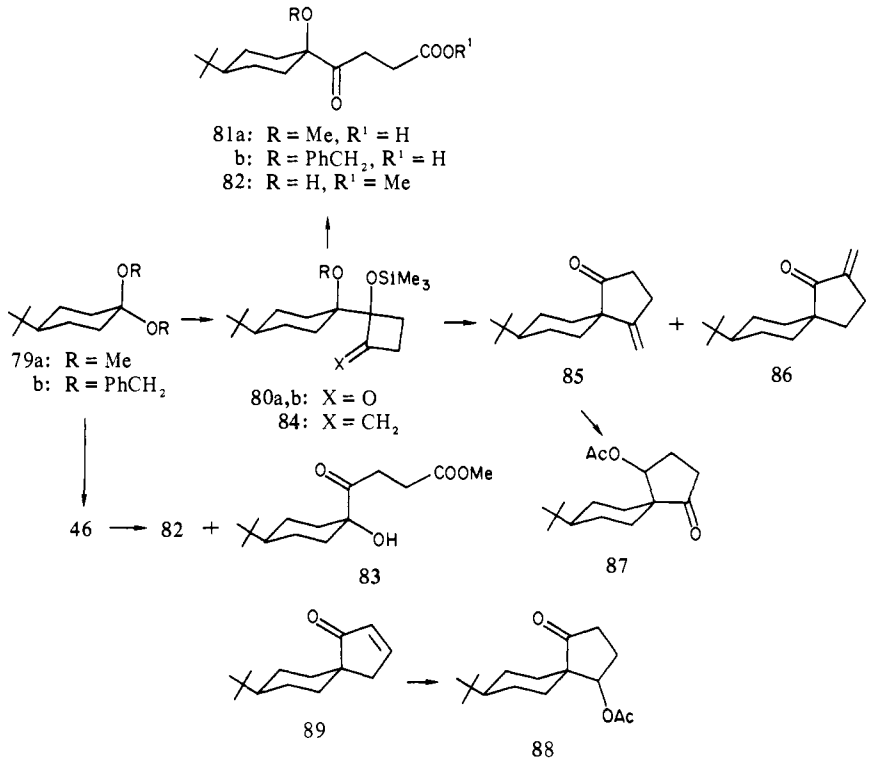
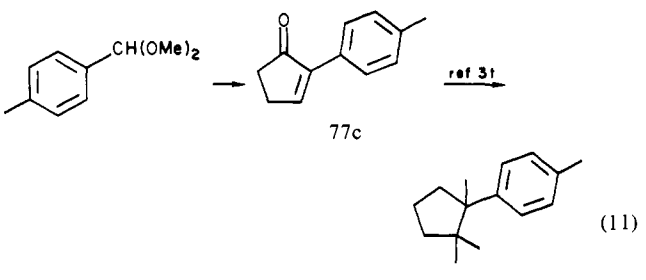


Table VI. Cyclopentenone Synthesis

series	$RCH(OMe)_2$, R =	% yield (diastereomers) aldol[a] (74)	% yield (diastereomers) wittig (75)	% yield ($t_{1/2}$)[f] rearr.
a	*n*-C_3H_7CH=CH (t)	100 (nd)	90 (nd)[c]	80 (<2 min)
b	C_6H_5CH=CH	76 (7:3)[b]	88 (nd)[c]	97 (<1 min)
c	*p*-$CH_3C_6H_4$	100 (8:2)	83 (8:2)[c]	90 (<1 min)
d	C_6H_5	93 (2:1)[b]	78 (7:3)[d]	81 (2.5 min)
e	*p*-ClC_6H_4	87 (8:2)	76 (7:3)[e]	83 (7 min)

[a] $TiCl_4$ catalyzed unless otherwise noted. [b] BF_3·Et_2O catalyzed. [c] $Ph_3PCH_3^+Br^-$/KH in THF. [d] $Ph_3PCH_3BF_4^-$/KH in THF. [e] $Ph_3PCH_3^+Br^-$/*tert*-AmOK in reflxg toluene. [f] Half-life of 75 determined at 35 °C with 40 equiv of TFA by ^1H NMR.

aromatic and unsaturated acetals (**75**, R = aryl or alkenyl) underwent a remarkably clean ring enlargement reaction to give, this time, cyclopentenone **77** (Table VII). The product was presumed to arise from the isomerization of the exo-olefinic isomer **76**, and in fact accumulation of **76e** was observed by ^1H NMR monitoring of the reaction mixture (Figure 1). The reaction rate (Table VI) showed clear dependence on the ability of the R group to stabilize cationic charge, and was much higher than that of the TFA catalyzed rearrangement of the parent **74**. The reaction sequence starting from *p*-tolualdehyde constitutes a short formal synthesis of *dl*-cuparene **78** (eq 11), since **77c**, available now in



(11)

75% overall yield from the acetal, has previously been converted to this sesquiterpene.[31]

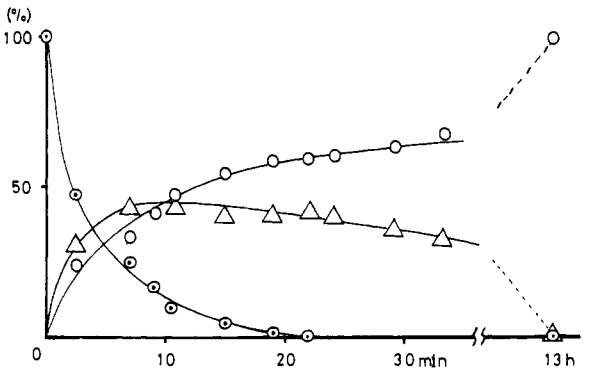


Figure 1. Conversion of **75e** to **77e** via **76e** (40 equiv of TFA, 35 °C: ⊙, % remaining **75e**; △, % yield of **76e**; ○, % yield of **77e**.

Having established the generality of the method, we then examined the stereochemistry of the reactions. 4-*tert*-Butylcyclohexanone dimethyl ketal (**79a**) was studied first (Scheme III), for this represents a conformationally fixed yet the least sterically biased substrate among cyclic ketals. The coupling of the ketal and **1** under BF_3·Et_2O catalysis quantitatively afforded **80a** as a single isomer. GLC analysis as well as ^1H NMR analysis confirmed the purity of the adduct. Keto acid **81a** obtained by oxidation[16] was also a single compound.

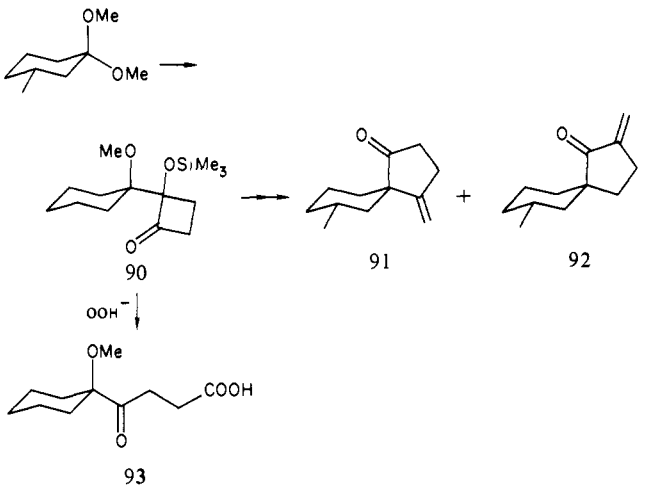
The attachment of the cyclobutyl group cis to the *tert*-butyl group seemed warranted in view of the known equatorial preference of carbon nucleophiles in the reaction with ketones,[32] but no solid data have ever been available for the Lewis acid catalyzed aldol reaction.[33] We therefore worked on the confirmation of the structure of **80**. To this end, we took dibenzyl ketal **79b** and converted it to **82**, since both demethylation of **80b** and methylation of authentic **82** under a variety of conditions failed. For instance,

(31) (a) DeMayo, P.; Suan, R. *J. Chem. Soc., Perkin Trans.* **1974**, 2559. (b) Kametani, T.; Tsubuki, M.; Nemoto, H. *Ibid.* **1980**, 759.

(32) (a) Ashby, E. C.; Jaemmle, J. T. *Chem. Rev.* **1975**, *75*, 521. (b) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540. Anh, N. T. *Top. in Curr. Chem.*, **1980**, *88*, 145. (d) Boone, J. R.; Ashby, E. C. *Top. Stereochem.* **1979**, *11* 53.

(33) Mukaiyama, T.; Hayashi, M. *Chem. Lett.* **1974**, 15.

Scheme IV



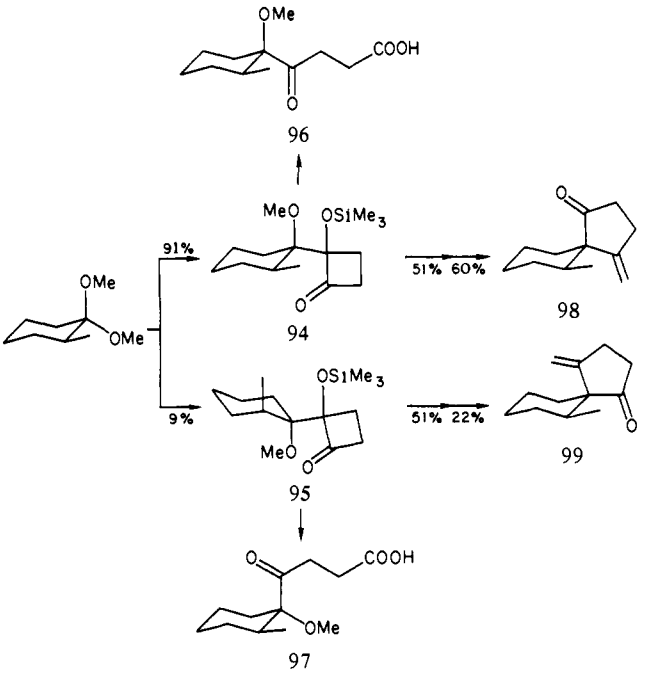
attempted demethylation of **80a** with BBr_3 produced a tertiary bromide due to demethoxylation. The reaction of **1** with dibenzyl ketal **79b** gave **80b** again as a single isomer, which on oxidation, esterification, and debenzylation gave hydroxy keto ester **82**. An authentic sample of **82** was prepared from **79a** via a sequence involving reductive succinoylation. MCPBA oxidation of **46** gave a 62:38 mixture of isomers. The major isomer was assigned as the axial alcohol **82** on the basis of TLF behavior (less polar)[35] in addition to the known axial preference of this epoxidation reaction.[34] Of these two isomers, the major isomer was identical with the product **82** obtained from **80b**. The perfect equatorial selectivity of the aldol coupling is thus established.[36] With the result of the highly selective aldol reaction in hand, we then proceeded to examine the ring enlargement. The Wittig reaction performed on crude **80a** gave **84** in over 90% yield (from the ketal). TFA treatment gave **85** and **86** in 49 and 4% yield, respectively. Detailed examination of the product mixture revealed the absence of stereoisomers of **85**. While the stereochemical assignment of **86** is tentative, that of the desired major product **85** was proved by conversion to **87**, followed by comparison with an authentic sample of the stereoisomer **83** prepared from **84**[37] (see the Experimental Section).

The foregoing set of experiments demonstrated the high stereoselectivity of the initial C–C bond formation and the excellent stereospecificity (inversion) of the second C–C bond forming rearrangement, culminating in the stereoselective construction of the quaternary center.

3-Methylcyclohexanone ketal is an interesting case to study in view of its conformational flexibility. The aldol reaction gave only two compounds as a 1:1 mixture, which on oxidation gave a *single* keto acid, **93**, of over 97% purity. The above-mentioned stereochemical results as well as the generality of the equatorial preference revealed for the simpler cases[36] indicated the structure **90**. The standard two-stage reaction gave the spiro ketone **91** as a single stereoisomer (52% yield from the ketal) along with the enone **92** (10%).

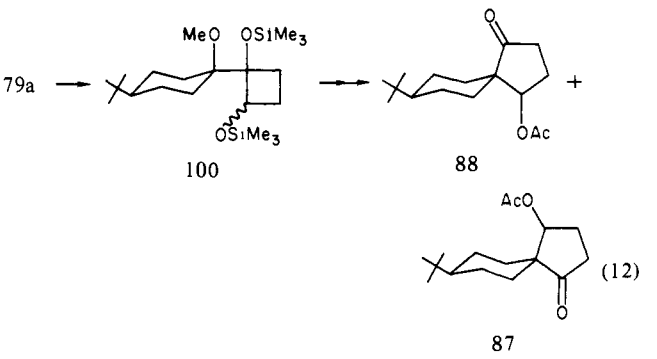
The reaction of 2-methylcyclohexanone dimethyl ketal in the presence of 0.5 equiv of $BF_3{\cdot}Et_2O$ gave a mixture of four diastereomers in a ratio of 84:11:4:1 in 94% combined yield (Scheme V). MPLC purification readily separated the mixture into two groups, **94** and **95**. Alternatively, use of 1 equiv of the catalyst

Scheme V



effected selective conversion of the minor isomer (**95**) to the ring-opened product, giving **94** exclusively in 73% yield. Oxidation of each pair with basic hydrogen peroxide gave **96** and **97**, respectively, indicating that the isomers in both **94** and **95** are diastereomeric with respect to the relative stereochemistry at the carbon and to the carbonyl group. The assignment of the structures of **94** and **95** relied on the ^{13}C NMR, on which the ring methyl groups of both **95a** and **95b** (14.74 and 15.79 ppm) appear higher than those of the isomeric **94a** and **94b** (16.64 and 16.73 ppm).[28] This stereochemistry is also predicted from the general tendency in such a system.[36] The reasons for the slightly decreased equatorial preference in this particular case and the predominance of one diastereomer of the four are presently unclear. Performance of the Wittig reaction and the rearrangement of **94** and **95** gave **98** and **99**, respectively, without any crossover. Small amounts of enone products corresponding to **62** were also produced. *These results conclusively demonstrate the complete inversion of the stereochemistry during the rearrangement.*

The highly stereoselective aldol reaction of cyclobutene **1** makes yet another type of spiro compounds available with a high degree of stereocontrol (eq 12). The triol-type system **100** prepared by



lithium aluminum hydride reduction and silylation was treated with $SnCl_4$ as previously described.[22] The [1,2] rearrangement of the siloxymethylene group proceeded cleanly (76%), producing a 62:1 mixture of **88** and **87** (after acetylation). The rearrangement is again highly stereospecific (with inversion).

Mechanistic Considerations. The reactions of three types of cyclobutanes described above exhibit some mechanistically intriguing points: (1) the distinct catalyst-dependent dichotomy in the reaction of the cyclobutanone **2a**, (2) the regioselectivity

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(36) The high equatorial selectivity in such an Lewis acid catalyzed reaction of *ketals* is general: Nakamura, E.; Horiguchi, Y.; Shimada, J.; Kuwajima, I. *J. Chem. Soc., Chem. Commun.* **1983**, 796.

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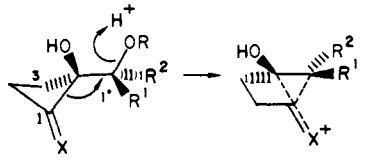
of the ring enlargement reactions, and (3) the high stereospecificity of the rearrangement of **2b** and **2c**.

Consider first the ring enlargement of **2a**. Though a number of reactions may be expected to occur on treatment of this multifunctional compound with an acid, only two processes were observed. The first reaction, the selective departure of the alkoxide at C-1′, avoids the formation of a cation next to the carbonyl group,[38] which would be the consequence of an alternative pathway (i.e., the ionization at C-2 cf. eq 13). This consideration, however, may be of questionable importance since the methylene cyclobutane **2b** also ionizes at C-1′ while the allylic C–O bond at C-2 appears more labile even if we allow for the neighboring group effect of the C-1 olefin in the ionization at C-1′.[39] In any event, the C-2 ionization is the only process that results in the ready release of the four-membered ring strain.

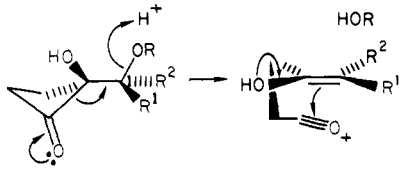
The highly selective migration of the carbonyl carbon (C-1)[40] following the cation formation is a rather peculiar consequence in the pinacol rearrangement, since the inductive effect of the carbonyl group would favor the migration of the C-3 methylene group. In fact, a considerable percentage of the C-3 migrates when the C-1 carbonyl group is replaced by a (less electron-withdrawing!) hydroxymethyne group.[22] The carbonyl participation theorem[41] (eq 13, X = O) and a fragmentation–recombination



(13)

101a: X = O
b: X = CH_2

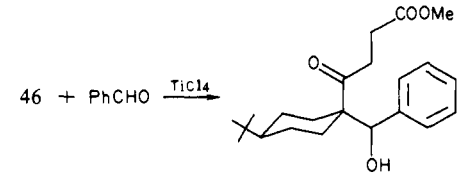
pathway (eq 14) may be invoked to account for the observed selectivity.



(14)

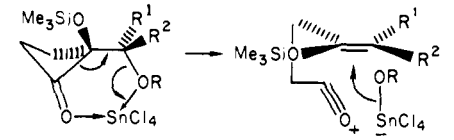
The first one (eq 13) assumes the development of a partial positive charge on oxygen as well as a very stringent arrangement[42] of the carbon atoms in the transition state **101a**. What appears more plausible is the second possibility (eq 14), which involves the acid-assisted Grob-type fragmentation[43] via the *antiperiplanar* arrangement of the leaving alkoxide and the cleaving C–C bond; the resulting cation is then trapped by the enol. Though the precise nature of this process, including the exact position of the transition state, is not clear, the notably long lifetime of enols[44] seems to allow even the involvement of a discrete enol species.

A picture related to eq 14 may rationalize the 62:1 selectivity observed for the production of **88** and **87**. If we assume a simple stepwise mechanism, the crucial C–C bond formation occurs before the rotation of the carbonyl-bearing side chain; a small amount of **87** then appears to represent a leak from the major pathway. External trapping of the enol silyl ether with an aldehyde was equatorially selective only to the extent of 90% (eq 15).



(15)

The nature of the acids influencing the dichotomy in the rearrangement of the cyclobutanone **2a** implies that the key to the reaction lies in the ligation of the metal to the substrate. When the substrate acts as a bidentate ligand as shown in eq 16, the



(16)

acyl cation generated by syn elimination[45,46] of the alkoxide is directly captured to form the keto ester (reductive succinoylation). The difficulty observed for ethylene and trimethylene ketals (leading to **51** and **52**) may have arisen from the presence of an extra internal ligand for the tin atom. The anomaly sometimes observed (cf. the behavior of **95**) implies that the alteration of the syn (eq 14) and anti (eq 15) pathways is also influenced by the configuration around the migrating center.

In view of the excellent stereospecificity with inversion, the ring enlargement of the methylene cyclobutane **2b** most likely conforms to the classical protocol of neighboring group participation[39,47] (eq 13, X = CH_2). The clean retention of the stereochemistry of the exo double bond during the rearrangement (eq 8) indicates that cationic **101b** is at best only short-lived. The relatively low regioselectivity (note that the conversion of **2a** to **3a** is perfectly regioselective) seems to reflect the stereochemical constraints in the bicyclic transition state **101b**.[42] The less substituted **75a–e** rearrange cleanly, while sterically more congested (at the migrating terminus) substrates tend to be much less selective (most notably in the production of **62**, **92**, etc.).

Conclusion

The results described in this paper have demonstrated the utility of the readily available succinoin derivatives **2** in organic synthesis. Application of the reaction has recently made possible concise syntheses of some terpenoids.[48,49] Extension of the basic idea of the ring expansion to larger rings was accomplisdhed recently[50] by using strictly aprotic conditions at the rearrangement stage. Similar approach under protic conditions exhibited some interesting anomalous behavior.[51]

Experimental Section

General Data. Melting points determined in glass capillaries and boiling points are uncorrected. Infrared (IR) spectra were recorded on a Hitachi EPI-G3 or 260-10 spectrometer; absorptions are reported in cm^{-1}. Proton nuclear magnetic resonance spectra (^1H NMR) were obtained as dilute CCl_4 solutions unless otherwise noted on a Hitachi R-24B, Varian Associate Model T-60, or a JEOL JNM-FX-100 spectrometer; the chemical shifts (δ) are expressed in parts per million downfield from internal tetramethylsilane. ^{13}C NMR spectra were obtained on a JEOL JNM-FX-100 or 90 spectrometer and chemical shifts are reported in parts per million downfield from internal tetramethylsilane. Gas–liquid chromatography (GLC) was performed on a Hitachi 163 instrument with a flame ionization detector and nitrogen carrier gas. Column

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(51) Pattenden, G.; Teague, S. *Tetrahedron Lett.* **1982**, *23*, 1403.

Table VII. Coupling of 1 and Carbonyl Compounds at −78 °C

carbonyl					adduct		
compd	g, mmol	1, g, mmol	catalyst, g, mmol	reacn time, h	compd	g, % yield	bp °C (mmHg)
benzaldehyde dimethyl acetal	1.07, 7.00	1.95, 8.40	$TiCl_4$ 1.19, 6.30	0.15	9	1.78, 91	-
p-chlorobenzaldehyde dimethyl acetal	0.150, 0.801	0.223, 0.961	$TiCl_4$ 1.36, 0.721	0.15	10	0.218, 87	-
p-tolualdehyde dimethyl acetal	0.570, 3.43	0.956, 4.12	$TiCl_4$ 0.59, 3.1	0.15	11	1.00, 100	-
cinnamaldehyde dimethyl acetal	0.446, 2.50	0.700, 3.01	$TiCl_4$ 0.31, 2.25	0.15	12	0.585, 76	-
(*E*)-2-hexenal dimethyl acetal	0.529, 3.67	1.03, 4.44	$TiCl_4$ 0.62, 3.30	0.15	13	1.01, 90	-
hexanal dimethyl acetal	1.74, 10.0	2.53, 11.0	$TiCl_4$ 1.89, 10.0	1.0	14	2.54, 89	95–98, 0.07
decanal dimethyl acetal	0.769, 3.34	0.789, 3.43	$TiCl_4$ 0.60, 3.00	1.0	15	1.033, 90	100–105, 0.06
3-pentanone dimethyl ketal	2.24, 17.0	4.14, 18.0	$BF_3 \cdot Et_2O$ 2.40, 16.9	1.0	16	4.04, 92	78–82, 0.5
cyclohexanone dimethyl ketal	1.44, 10.0	2.79, 12.0	$BF_3 \cdot Et_2O$ 1.24, 9.0	0.2	17	2.45, 90	-
cyclohexanone diethyl ketal	0.327, 1.90	0.437, 1.90	$BF_3 \cdot Et_2O$ 0.267, 1.88	1.5	18	0.485, 90	85–90, 0.05
cyclooctanone dimethyl ketal	3.78, 22.0	4.60, 20.0	$BF_3 \cdot Et_2O$ 2.52, 22.0	1.0	19	4.18, 70	105–112, 0.1
cyclododecanone dimethyl ketal	1.94, 8.50	2.02, 8.80	$BF_3 \cdot Et_2O$ 1.18, 8.34	1.5	20	2.77, 92	135–150, 0.7
2-allylcyclohexanone dimethyl ketal	0.425, 2.30	0.601, 2.60	$BF_3 \cdot Et_2O$ 0.28, 2.0	0.15	21	0.617, 87	-
norbornanone dimethyl ketal	0.242, 1.55	0.345, 1.50	$BF_3 \cdot Et_2O$ 0.214, 1.51	0.5	22	0.253, 60	95–100, 0.07
4-*t*-butylcyclohexanone dimethyl ketal	5.11, 25.7	6.50, 28.0	$BF_3 \cdot Et_2O$ 2.82, 22.9	0.5	80a	8.94, 100	-
3-methylcyclohexanone dimethyl ketal	1.20, 7.00	1.76, 7.70	$BF_3 \cdot Et_2O$ 0.43, 3.5	0.15	90	2.15, 100	-
2-methylcyclohexanone dimethyl ketal	1.20, 7.00	1.73, 7.70	$BF_3 \cdot Et_2O$ 0.43, 3.5	0.3	94 95	1.71, 86 0.173, 8	- -

A refers to a fused silica capillary column (20 m) coated with OV-101 and column B to a column (3 mm × 2 m) packed with 10% PEG-20M on 60–80 mesh Diasolid L. Mass spectra (MS) were determined on a Hitachi RMU-7M or a Shimazu LKB 9000 (GC-MS equipped with a column packed with OV-17) instrument at an ionization potential of 70 eV. Microanalyses were performed on a Perkin-Elmer 240 at the Microanalytical Laboratory, Tokyo Institute of Technology. Purification of the products was achieved either by preparative TLC with glass plates (20 × 20 cm) coated with Merck Kieselgel PF_{254} or by flash chromatography[52] with Wako gel C-300 previously washed by water to remove fine and coarse particles.

The reactions were usually carried out under nitrogen. Organic extracts were dried over $MgSO_4$ and concentrated by a rotary evaporator. Bulb-to-bulb distillation was performed with a Kugelrohr apparatus.

1,2-Bis(trimethylsiloxy)-1-cyclobutene (1). The reaction of molten potassium–sodium alloy (39.9 g of potassium and 23.4 g of sodium), diethyl succinate (87.6 g, 0.50 mol), and chlorotrimethylsilane (244 g, 2.24 mol) according to the reported method[3] gave 90.6 g (78%) of the title compound; bp 72–73 °C (8 mm).

2-Phenyl-1,3-cyclopentanedione (23) from Benzaldehyde Diethyl Acetal. General Procedure for Geminal Acylation. To a cooled (−78 °C) mixture of $BF_3 \cdot Et_2O$ (1.45 g, 10.2 mmol) and benzaldehyde diethyl acetal (1.98 g, 11.0 mmol) in 10 mL of methylene chloride was added dropwise a solution of **1** (2.76 g, 12.0 mmol) in 5 mL of methylene chloride. The colorless mixture was stirred for 3 h and poured into aqueous $NaHCO_3$. The organic layer was extracted with ether, and the ethereal extract was dried and concentrated to afford 3.31 g of an oily product, from which 2.97 g (92.5%) of **8** was obtained by distillation as a 1:2 diastereomeric mixture: bp 135–137 °C (9 mm); IR (neat) 1795 (s), 1258 (s), 870 (s), 844 (s); ^1H NMR 0.10 (s, 9 H), 1.27 (t, 2 H), 1.33 (t, J = 7 Hz, 1 1.5-3.0 (m, 4 H), 3.3–4.0 (m, 2 H), 4.45 (s, 1 H, OCH), 7.39 (s, 1.7 H), and 7.44 (s, 3.3 H, C_6H_5); MS, *m/e* (relative intensity) 292 (M^+, 2), 264 (1), 236 (3), 219 (5), 218 (6), 207 (5), 206 (6), 174 (4), 135 (26), 129 (14), 118 (16), 107 (25), 79 (22), 77 (14), 75 (24), 73 (100), 45 (26).

The above cyclobutanone (290 mg, 0.993 mmol) was treated with refluxing TFA (3 mL) for 15 min. The brown mixture was diluted with methanol, treated with charcoal, and filtered. Concentration afforded a pale yellow crystalline product (162 mg, 93.7%), which melted at 227–229 °C. Recrystallization from ethyl acetate gave an analytical sample: mp 231–232 °C (lit.[53] 233–234 °C, 247 °C[54]); IR (KBr) 2700–2030 (br), 2030–1700 (br), 1555 (m), 1360 (vs), 1297 (vs); ^1H NMR (TFA) 2.35 (s, 1 H), 3.03 (s, 4 H), 7.44 (s, 5 H). Anal.

Preparation of 23 from Benzaldehyde. To a mixture of benzaldehyde and $TiCl_4$ (424 mg, 2.23 mmol) in 4 mL of methylene chloride at −78 °C was added a solution of **1** (575 mg, 2.50 mmol) in 5 mL of methylene chloride, and the dark mixture was stirred for 30 min at −78 °C. Water was added and the product obtained by extraction (555 mg) was pure by TLC and NMR (78%): ^1H NMR 0.11 (s, 9 H), 1.65–2.8 (m, 4 H), 3.08 (s, 1 H, OH), 4.71 (s, 1 H), 7.32 (s, 5 H).

The crude **6** was treated with 3 mL of TFA for 2 h at 30 °C. The mixture was worked up as above to give **23** (294 mg, 76% overall yield).

Spectral Properties of Cyclobutanones 2a. The cyclobutanones were characterized by spectroscopy and subjected to the subsequent reactions without rigorous purification.

2-(Methoxyphenylmethyl)-2-(trimethylsiloxy)cyclobutanone (9): ^1H NMR 0.15 (s, 9 H), 1.5–3.0 (m, 4 H), 3.29 (s, 3 H), 4.29 (s, 1 H; this signal separated in 25% benzene/CCl_4 into two singlets of 8:2 relative intensity), 6.9–7.4 (m, 5 H).

2-[(4-Chlorophenyl)methoxymethyl]-2-(trimethylsiloxy)cyclobutanone (10): IR (neat) 1780 ns), 1245, 1095, 840; ^1H NMR 0.15 (s, 9 H), 1.5–3.0 (m, 4 H), 3.25 (s, 3 H, OMe), 4.20 (s, 1 H; separates into two singlets of 8:2 intensities with 25% benzene), 7.26 (s, 4 H).

2-[(4-Methylphenyl)methoxymethyl]-2-(trimethylsiloxy)cyhclobutanone (11): IR (neat) 1780, 1250, 1100, 850; ^1H NMR 0.13 (s, 9 H), 1.3–3.0 (m, 7 H, involving singlet at 2.40), 3.25 (s, 3 H, OMe), 4.13 (s, 1 H, two singlets of 8:2 intensities with 25% benzene), 7.1–7.2 (m, 4 H).

2-(3-Phenyl-1-methoxy-(*E*)-2-propenyl)-2-(trimethylsiloxy)cyclobutanone (12): IR neat) 1770 (s), 1250, 1010, 820; ^1H NMR 0.12 (s. 9 H), 1.0–2.9 (m, 4 H), 2.65 (s, 3 H, OMe), 3.57 (s, 0.7 H), 3.75 (s, 0.3 H), 5.6–6.6 (m, 2 H), 6.9–7.2 (m, 5 H).

2-(1-Methoxy-(*E*)-2-hexenyl)-2-(trimethylsiloxy)cyclobutanone (13): IR (neat) 1770 (s), 1650, 1250, 100, 860; ^1H NMR 0.09 (s, 9 H), 0.6–2.9

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Table VIII. Preparation of 1,3-Cyclopentanediones

no.	aldol adduct, g, mmol	TFA, mL	condtns °C, h	no.	product, g, % yield	bp (mm), °C (mp, °C)
14	2.07, 7.23	10	reflux, 20	24	0.95, 78	(136)
16	0.483, 1.87	2	25, 2	26	0.234, 87	70 (0.06)
18	0.480, 1.69	2	30, 1.5	27	0.248, 88	75–80 (0.05) (61–62)
20	2.55, 7.20	3	25, 1	28	1.69, 94	(116.5–117)
22	0.223, 0.79	2	25, 1	31	0.129, 92	(109.5–110.5)

(m, 13 H), 3.14 (s, 3 H, OMe), 3.46 (d, 1 H), 5.0–5.8 (m, 2 H).

2-(1-Ethoxyhexyl)-2-(trimethylsiloxy)cyclobutone (14): IR (neat) 1780, 1250, 1095, 850; ^{1}H NMR 0.11 (9 H), 0.6–2.9 (m, 15 H), 3.0–3.2 (m, 3 H).

2-(1-Ethoxydecyl)-2-(trimethylsiloxy)cyclobutanone (15): ^{1}H NMR 0.11 (s, 9 H), 0.7–3.0 (m, 26 H), 3.1–3.8 (m, 3 H).

2-(1-Ethyl-1-methoxypropyl)-2-(trimethylsiloxy)cyclobutanone (16): IR (neat) 1791 (s), 1252 (s), 897 (s), 845 (s); ^{1}H NMR 0.11 (s, 9 H), 0.88 (t, J = 7 Hz, 6 H, CH_3), 1.45–1.9 (m, 5 H), 2.3–3.0 (m, 3 H, cyclobutane), 3.25 (s, 3 H); MS m/e (relative intensity) 258 (M^+, 2), 243 (3), 229 (6), 215 (10), 202 (18), 201 (18), 187 (22), 171 (14), 101 (47), 75 (30), 73 (100), 57 (39), 45 (48).

2-(1-Methoxycyclohexyl)-2-(trimethylsiloxy)cyclobutanone (17): IR (neat) 1780 (s), 1260, 1080 (s), 860 (s); ^{1}H NMR 0.07 (s, 9 H), 0.9–2.9 (m, 14 H), 3.20 (s, 3 H).

2-(Ethoxycyclohexyl)-2-(trimethylsiloxy)cyclobutanone (18): IR (neat) 1789 (s), 1250 (s), 1070 (s), 843 (s); ^{1}H NMR 0.11 (s, 9 H), 0.9–2.2 (m, involving a triplet, J = 7 Hz at 1.10), 2.2–2.9 (m, 3 H), 3.2–3.7 (AB part of ABX_3, 2 H, CH_2O).

2-(1-Methoxycyclooctyl)-2-(trimethylsiloxy)cyclobutanone (19): IR (neat) 1780 (s), 1250, 850 (s); ^{1}H NMR 0.13 (s, 9 H), 1.0–2.9 (m, 18 H), 3.16 (s, 3 H).

2-(1-Methoxycyclododecyl)-2-(trimethylsiloxy)cyclobutanone (20): IR (neat) 1781 (s), 1252 (s), 845 (s); ^{1}H NMR 0.11 (s, 9 H), 1.0–2.1 (m, 26 H), 2.25–2.9 (m, 3 H, cyclobutane), 3.25 (s, 3 H); MS m/e (relative intensity) 354 (M^+, 4), 339 (3), 326 (9), 312 (7), 311 (5), 298 (24), 297 (10), 283 (5), 267 (8), 197 (46), 75 (32), 73 (100), 55 (77), 41 (57).

2-(2-Allyl-1-methoxycyclohexyl)-2-(trimethylsiloxy)cyclobutanone (21): IR (neat) 3040, 2910, 1775, 1630, 1250, 840; ^{1}H NMR 0.22 (s, 9 H), 1.0–2.9 (m, 15 H), 3.10 (s, 3 H), 4.77 (m, 1 H), 5.00 (d, 1 H, J = 4.5 Hz), 5.4–6.1 (m, 1 H).

2-Methoxy-2-(2-oxo-1-(trimethylsiloxy)cyclobutyl)bicyclo[2.2.1]heptane (22): IR (neat) 1786 (s), 1240 (s), 845 (s); ^{1}H NMR 0.10 (s, 9 H), 0.9–3.0 (m, 14 H), 3.16 (s, 0.13 H), 3.28 (s, 0.87 H); MS m/e (relative intensity) 282 (M^+, 4), 267 (2), 254 (4), 253 (4), 240 (5), 239 (5), 226 (36), 211 (16), 125 (47), 93 (40), 73 (100), 45 (30).

2-(*c*-4-*tert*-Butyl-*r*-1-methoxycyclohexyl)-2-(trimethylsiloxy)cyclobutanone (80a): GLC retention time, 6.7 min (>98% pure, column A, 200 °C); IR (neat) 1780 (s), 1245, 1170 (s), 845 (s); ^{1}H NMR 0.06 (s, 9 H), 0.80 (s, 9 H), 0.9–3.0 (m, 12 H), 3.19 (s, 3 H).

2-(*c*-3-Methyl-*r*-1-methoxycyclohexyl)-2-(trimethylsiloxy)cyclobutanone (90): GLC retention time 7.9 min (single peak by column A, 170 °C); IR (neat) 1778 (s), 1245, 1170 (m), 845 (s); ^{1}H NMR 0.06 (s, 9 H, 0.7–2.9 (m, 16 H, involving doublets at 0.79 and 0.83, J = 7 Hz, of equal intensities), 3.12 (s, 3 H).

Spectral Properties of Cyclopentanediones (3a). 2-Pentyl-1,3-cyclopentanedione (24a): IR (KBr) 3540–2000, 2000–1760, 1540, 1535, 1430, 1360, 1265, 1125, 665; ^{1}H NMR (TFA) 0.80–1.2 (distorted, distorted t, 3 H), 1.2–2.8 (m, 9 H), 3.10 (s, 4 H). This compound was treated sequentially with diazomethane and methyllithium to give dihydrojasmone in 76% yield.[55]

2-Nonyl-1,3-cyclopentanedione (25): IR (KBr) 3540–2000 (m, br), 2000–1760 (s, br), 1547 (s), 1535 (s), 1430 (s), 1360 (vs), 1262 (s), 1128 (s), 664 (m); ^{1}H NMR (TFA) 0.7–1.1 (distorted t, 3 H), 1.1–1.8 (m, 14 H), 2.2–2.6 (m, 2 H), 3.10 (s, 4 H). Anal. ($C_{14}H_{24}O_2$): C, H.

2,2-Diethyl-1,3-cyclopentanedione (26): IR (neat) 1724 (s); ^{1} NMR 0.75 (t, J = 7 Hz, 6 H), 1.63 (q, J = 7 Hz), 2.65 (s, 4 H); MS, m/e (relative intensity) 154 (M^+, 55), 139 (81), 126 (9), 111 (25), 97 (39), 83 (66), 55 (100), 41 (47), 39 (40), 29 (35), 28 (30), 27 (47). Anal. Calcd for $C_8H_{14}O_2$: 154.0993. Found: 154.1023.

Spiro[4.5]decane-1,4-dione (27): IR (neat) 1720 (vs); ^{1}H NMR 1.58 (br s, 10 H), 2.65 (s, 4 H); MS, m/e (relative intensity) 166 (M^+, 100), 137 (24), 124 (36), 112 (87), 111 (83), 109 (27), 85 (38), 81 (48), 67 (95), 56 (48), 54 (45), 53 (42), 41 (58), 30 (64); alcd for $C_{10}H_{14}O_2$, 166.0994; found, 166.0983. Anal. ($C_{10}H_{14}O_2$): C, H.

(55) Inoue, T.; PhD Thesis, Tokyo Institute of Technology, 1980.

Spiro[4.11]hexadecane-1,4-dione (28): IR (KBr) 1752 (w), 1717 (s); ^{1}H NMR ($CDCl_3$) 1.43 (r s, $W_{1/2}$ = 3 Hz) and 1.53 (br s, 22 H), 2.75 (s, 4 H); MS, m/e (relative intensity) 250 (M^+, 23), 125 (39), 112 (100), 69 (33), 67 (39), 55 (76), 41 (91). Anal. ($C_{16}H_{26}O_2$): C, H.

5,8-Methanospiro[4.5]decane-1,4-dione (31): IR (KBr) 1760 (w), 1717 (s); ^{1}H NMR 1.05–2.05 (m, 8 H), 2.40 (br s, 2 H), 2.5–2.8 (m, 4 H); MS, m/e (relative intensity) 178 (M^+, 27), 149 (57), 112 (100), 93 (40), 79 (30), 77 (20), 67 (29), 66 (28), 65 (31), 55 (25), 53 (26), 41 (27), 39 (44), 29 (25). Anal. ($C_{11}H_{14}O_2$): C, H.

4-Cyclododecyl-4-oxobutanoic Acid (32). The diketone **28** (250 mg, 1.0 mmol) was heated in 1 N methanolic sodium hydroxide for 30 min. The mixture was acidified with concentrated HCl and extracted with ether to give a yellow crystalline product (269 mg). Recrystallization from hexane/benzene gave a pure sample (164 mg, 62%): mp 117.5–118.5 °C; bp 140–150 °C (bath temperature) (0.05 mm); IR (KBr) 3600–2300 (br), 1719 (s), 1701 (s); ^{1}H NMR ($CDCl_3$) 1.0–1.8 (m, 22 H), 2.5–2.9 (m, 5 H), 9.00 (br, 1 H). Anal. ($C_{16}H_{28}O_3$): C, H.

Preparation of the Cyclic Ketal 34. A solution of 2-((methoxycarbonyl)methyl)cyclohexanone (3.10 g, 18.2 mmol) in 50 mL of dry methanol was refluxed for 10 h with trimethyl orthoformate (11.9 g, 0.11 mol) and *p*-toluenesulfonic acid (0.9 g). After neutralization and extractive workup 3.8 g (96%) of the ketal was obtained: IR (neat) 1740; ^{1}H NMR 1.0–2.0 (m, 9 H), 2.27 (s, 2 H), 3.07 (s, 6 H), 3.57 (s, 3 H).

The ketal (3.70 g, 17 mmol) was reduced with lithium aluminum hydride (LAH) (0.097 g, 26 mmol) in ether to give 3.0 g (89%) of the reduced material: IR (neat) 3350, 2930, 1440, 1110; ^{1} NMR 3.07 (s, 6 H), 3.53 (t, 2 H, J = 9 Hz).

A solution of the alcohol (7.5 g, 40 mmol) in 50 mL of methylene chloride was treated with a small amount of pyridinium *p*-toluenesulfonate to obtain 4.7 g (75%) of **34** by distillation: bp 50 °C (12 mm); IR (neat) 2930, 1440, 1250, 1090, 925; ^{1}H NMR (CCl_4) 0.7–2.4 (m, 11 H), 3.07 (s, 3 H), 3.5–3.9 (m, 2 H).

Preparation of the Hemiketal 38. To a solution of TMSOTf (1.2 ml, 6.4 mmol) in 10 mL of methylene chloride was added a mixture of the ketal **34** (1.0 g, 6.4 mmol) and **1** (1.5 g, 6.4 mmol). Extractive workup gave 1.77 g (98%) of **35**: IR (neat) 1775; ^{1}H NMR 0.11 (s, 9 H), 1.0–2.9 (m, 15 H), 3.5–4.0 (m, 2 H).

The adduct **35** (600 mg, 2.13 mmol) was treated with TFA (4.9 mL) for 3.5 h at room temperature to produce two compounds. The minor component (R_f = 0.30, 20% ethyl acetate in hexane) was the trifluoroacetate **37** and the major one (R_f = 0.16) was the tricyclic **38**. The mixture of the products was treated with methanolic K_2CO_3 to give 298 mg (70%) of **38** as crystals: mp 105–106 °C (hexane); IR (KBr) 3380, 2900, 1720; ^{1}H NMR ($CDCl_3$) 1.0–2.6 (m, 1k *H*), 2.7–3.0 (m, 1 H), 3.4–4.2 (m, 2 H). Anal. ($C_{12}H_{18}O_3$): C, H.

37: IR (neat) 2920, 1770, 1450, 1220, 1160; ^{u}H NMR 1.2–2.1 (m, 12 H), 2.68 (d, J = 6 Hz, 4 H), 4.27 (t, J = 9 Hz).

Rearrangement of Cyclobutanone 39. The cyclobutanone **39** (102 mg, 0.33 mmol) was treated with 0.25 mL of TFA to give **40** (48.3 mg, 70%) and **41** (20.7 mg, 26%).

40: R_f 0.52 (20% ethyl acetate in hexane); IR (neat) 2900, 1.705, 1450, 1170; ^{1}H NMR 0.6–2.0 (m, 15 H), 2.57 (m, 4 H).

41: R_f 0.64; IR (neat) 2900, 1730, 1700, 1210; ^{1}H NMR 0.7–2.7 (m, 19 H), 3.58 (s, 3 H).

These compounds were identical with the samples prepared by hydrogenation of **29** and **30**.

Ethyl 4-Cyclohexyl-4-oxobutanoate (43). General Procedure for Reductive Succinoylation. To a stirred solution of $SnCl_4$ (7.50 g, 28.8 mmol) at −78 °C in 15 mL of methylene chloride was added over a 10-min period a mixture of cyclohexanone diethyl ketal (4.82 g, 28.0 mmol) and **1** (6.44 g, 28.0 mmol) in 10 mL of methylene chloride. The yellow solution was stirred for 15 min at −78 °C and at −30 °C for 15 min. Water was added, and the mixture was extracted twice with ether. The combined extracts were washed with 1 N HCl, saturated $NaHCO_3$, water, and saturated NaCl. The crude product (6.30 g) was distilled to an analytically pure sample of **43** (5.44 g, 93%): bp 110–112° (2.5 mm); IR (neat) 1739 (s), 1713 (s), 1872 (m), 1187 (m), 1167 (m); ^{1}H NMR 0.8–1.9 (m, 18 H, involving a triplet, J = 7 Hz at 1.28), 4.15 (q, J = 7 Hz 2 H); MS, m/e (relative intensity) 212 (M^+, 5), 167 (20), 129 (55),

Table IX. Reductive Succinoylation

ketal	g, mmol	1, g, mmol	$SnCl_4$ g, mmol	no.	product, g, mmol	bp, °C, mm Hg
3-pentanone dimethyl ketal	0.198, 1.50	0.357, 1.55	0.14, 0.54	42	0.240, 87	95-105, 22
cyclohexanone diethyl ketal	0.864, 5.02	1.163, 5.06	0.68, 0.26	44	1.215, 85	110-115, 0.04
2-allylcyclohexanone dimethyl ketal	1.20, 6.50	1.80, 7.80	1.70, 6.50	30	1.22, 70	105-106, 5
4-tert-butylcyclohexanone dimethyl ketal	0.424, 2.21	0.506, 2.20	0.166, 0.64	45	0.520, 92	100-105, 0.015
cyclopentanone diethyl ketal	3.20, 20.3	4.73, 2.06	5.0, 19.2	47	4.90, 89	100-110, 0.04
2-norbornanone dimethyl ketal	0.204, 1.30	0.372, 1.62	0.331, 1.27	48	0.253, 90	80-85, 0.015
cyclododecanone dimethyl ketal	0.417, 1.83	0.423, 1.84	0.460	49	0.468, 1.76	115-120, 0.015
adamantanone dimethyl ketal	0.275, 1.40	0.322, 1.40	0.361, 1.40	50	0.237, 68	120, 0.01
4-methyl-3-cyclohexen-1-one ethylene ketal	2.00, 13.0	5.52, 26.0	10.0, 38.5	51	1.46, 46	
4-methyl-3-cyclohexen-1-one trimethylene ketal	0.192, 1.14	0.524, 2.28	0.598, 2.29	52	0.156, 54	

111 (28), 101 (80), 83 (100), 55 (72), 41 (37), 29 (34). Anal. ($C_{12}H_{20}O_3$): C, H.

Methyl 4-(4-*tert*-Butylcyclohexylidene)-4-(trimethylsiloxy)butanoate (46): Triethylamine Quench. To a stirred solution of $SnCl_4$ (0.03 ml, ca. 0.3 mmol) in 2.5 mL of methylene chloride at −78 °C was added a solution of 4-*tert*-butylcyclohexanone dimethyl ketal (604 mg, 3.02 mmol) and **1** (696 mg, 3.30 mmol) in 2 mL of methylene chloride over 20 s. After stirring for 5 min at −78 °C, triethylamine (0.33 mL) and 20 mL of hexane were added. The suspension was filtered under nitrogen, and the filtrate was washed with water, 1 N HCl, and saturated $NaHCO_3$. After drying and concentration 827 mg of **46** was obtained as an oil (84%): R_f 0.5 (benzene); IR (neat) 1747 (s), 1676 (w), 1253 (s), 865 (s), 843 (s); ^1H NMR 0.16 (s, 9 H), 0.6–2.5 (m, 22 H, involving singlets at 0.84 and 2.35), 3.56 (s, 3 H). Anal. Calcd for $C_{18}H_{34}SiO_3$: 326.2275. Found: 326.2263.

Spectral Properties of γ-Keto Esters. Methyl 4-(2-Allylcyclohexyl)-4-oxobutanoate (30): IR (neat) 2900, 1725, 1700, 1630, 1200, 1160, 910; ^1H NMR 1.0–2.2 (m, 11 H), 2.3–2.9 (m, 4 H), 3.58 (s, 3 H), 4.77 (1 H), 5.00 (m, 1 H), 5.4–6.1 (m, 1 H). Anal. ($C_{14}H_{22}O_3$): C, H.

Methyl 5-Ethyl-4-oxoheptanoate (42): IR (neat) 1743, 1718; ^1H NMR 0.84 (t, J = 7 Hz, 6 H), 1.35–1.9 (m, 4 H), 2.05–2.8 (m, 5 H, involving A_2B_2m centered at 2.52), 3.60 (s, 3 H); MS, *m/e* (relative intensity) 158 (M^+ − 28, 10), 155 (11), 115 (100), 99 (17), 87 (20), 71 (74), 55 (66), 43 (90).

Methyl 4-(4-*tert*-Butylcyclohexyl)-4-oxobutanoate (45): IR (neat) 1744 ns), 1712 (s), 1363 (m); ^1H NMR 0.6–2.9 (m, 23 H, involving two singlets at 0.82 and 0.89), 3.61 (s, 3 H). Anal. ($C_{15}H_{26}O_3$): C, H.

Methyl 4-(2-Norbornyl)-4-oxobutanoate (48): IR (neat) 1745, 1714; ^1H NMR 1.05–2.0 (m, 8 H), 2.2–3.1 (m, 7 H), 3.66 (s, 3 H). Anal. ($C_{12}H_{18}O_3$): C, H.

Methyl 4-Cyclododecyl-4-oxobutanoate (49): IR (neat) 1747 (s), 1713 (s); ^1H NMR 1.0–2.0 (m, 22 H), 2.25–2.85 (m, 5 H), 3.60 (s, 3 H); MS, *m/e* 282 (M^+). This keto ester gave acid **32** on basic hydrolysis.

Methyl 4-(2-Adamantyl)-4-oxobutanoate (50): IR (neat) 1741 (s), 1707 (s); ^1H NMR 1.5–2.2 (m, 12 H), 2.3–3.05 (m, 7 H), 3.69 (s, 3 H). Anal. ($C_{15}H_{22}O_3$): C, H.

2-Hydroxyethyl 4-(4-Methyl-3-cyclohexenyl)-4-oxobutanoate (51): IR (neat) 1730, 1705; ^1H NMR 1.5–3.0 (m, 14 H, involving broad singlets at 1.63 and A_2B_2 m at 2.3–3.0), 3.10 (br s, 1 H), 3.6–3.9 (A_2B_2 m, 2 H), 4.0–4.3 (A_2B_2 m, 2 H), 5.26–5.53.

This gave the same γ-lactone that was derived from **52** on reduction of the ketone function.

3-Hydroxypropyl 4-(4-Methyl-3-cyclohexenyl)-4-oxobutanoate (52): IR (neat) 3420, 1724, 1708; ^1H NMR 1.5–2.3 (m, 12 H, involving a broad singlet at 1.65), 1.88 (t, J = 6.3 Hz, 2 H), 2.61 (A_2B_2 m, 4 H), 3.18 (br s, 1 H), 3.58 (t, J = 6.3 Hz, 2 H), 4.13 (t, J = 6.3 Hz, 2 H), 5.34 (br s, 1 H).

This ester gave 4-hydroxy-4-(4-methyl-3-cyclohexenyl)butanoic lactone upon sodium borohydride reduction: bp 118–119 °C (bath temp) (0.45 mm); IR (neat) 1770 (s), 1180 (s); ^1H NMR 1.3–2.7 (m, 14 H), 3.9–4.4 (m, 1 H), 5.2–5.3 (m, 1 H). Anal. ($C_{11}H_{16}O_2$): C, H.

Methyl 4-(4-Methyl-3-cyclohexenyl)-4-pentenoate (54). The ester **52** (604 mg, 2.38 mmol) was hydrolyzed with sodium hydroxide to obtain 364 mg (74%) of the acid **53** as a solid: IR (CCl_4) 2400–3400 (br s), 1710 (vs); ^1H NMR 1.5–2.9 (m, 3 H, involving a broad singlet at 1.67), 2.67 (br s, 4 H), 5.40 (m, 1 H), 11.1 (br s, 1 H).

Dibromomethane (1.304 g, 7.49 mmol) in 6 mL of THF was added to a suspension of activated zinc (1.469 g, 22.5 mmol) in 10 mL of THF. After stirring for a while, 6.5 mL of a 1 M methylene chloride solution of $TiCl_4$ was added slowly. After 20 min, **43** (491 mg, 2.51 mmol) in 9 mL of THF was added and after 5 h at room temperature 2 mL of pyridine was added. The mixture was filtered and the filtrate was extracted with ether after acidification. The crude product was esterified with diazomethane to obtain 345 mg (66%) of **54** after purification: bp 95–97 °C (bath temperature) (0.35 mm); IR (neat) 1735 (s), 1640, 895, 800; ^1H NMR 1.5–2.2 (m, 10 H, involving a broad singlet at 1.60), 2.33 (br s, 4 H), 3.57 (s, 3 H), 4.68 (br d, J = 4 Hz, 2 H), 5.31 (br s, 1 H). Anal. ($C_{13}H_{20}O_2$): C, H.

2-(4-Methyl-3-cyclohexenyl)-1-penten-5-ol (55). The ester **54** (223 mg, 1.07 mmol) was reduced with LAH (50 mg, 1.3 mmol) in ether to obtain 164 mg (85%) of **55** after purification. The spectroscopic properties of this sample were identical with those reported:[18] bp 87–89 °C (0.8 mm); IR (neat) 3330 (br s), 3075 (w, C=CH_2), 1640 (m, C=C), 1056, 891, 800; ^1H NMR ($CDCl_3$) 1.5–2.3 (m, 15 H, involving broad singlets at 1.67 and 1.84), 3.63 (t, 2 H, J = 6 Hz), 4.76 (br s, 2 H, CH_2=F), 5.42 (br s, 1 H, CH=). Anal. ($C_{12}H_{20}O$): C, H.

Ethyl 4-[(1-Furylhydroxymethyl)cyclohexyl]-4-oxobutanoate (57). A mixture of 44 (602 mg, 2.12 mmol) and furfural (203 mg, 2.12 mmol) in 3.5 mL of THF was treated with 174 mg of tetrabutylammonium fluoride[12] at −78 to −20 °C. After HCl treatment and purification, 451 mg of **57** was obtained as an oil (67%): IR (neat) 3450 (br s), 1740 (s), 1710 (s); ^1H NMR 0.5–3.0 (m, 17 H, involving t, J = 7 Hz, at 1.23 and A_2B_2 m at 2.3–3.0), 3.5 (br s, 1 H), 4.13 (q, J = 7 Hz, 2 H), 4.63 (br s, 1 H), 6.07 (m, 2 H), 7.2–7.4 (m, 1 H). Anal. ($C_{17}H_{24}O_5$): C, H.

Ethyl 4-(1-(Phenylsulfenyl)cyclohexyl)-4-oxobutanoate (58). To a mixture of cyclohexanone diethyl ketal (347 mg, 2.02 mmol), **1** (467 mg, 2.03 mmol), and $SnCl_4$ (0.15 ml) in 2 mL of methylene chloride at −78 °C was added benzenesulfenyl chloride (301 mg, 2.08 mmol). Aqueous extractive workup followed by bulb-to-bulb distillation gave **43** (72 mg, 16%) and **58** (502 mg, 78%): bp 140–180 °C (bath temperature) (0.13 mm); IR (neat) 1733 (s), 1697 (s); ^1H NMR 1.0–2.2 (n, 10 H), 2.4–3.3 (A_2B_2 m, 4 H), 4.13 (q, J = 7 Hz), 7.27 (s, 5 H). Anal. ($C_{18}H_{24}O_3S$): C, H, S.

Ethyl 4-[1-(Hydroxyphenylmethyl)-2-methylcyclohexyl]-4-oxobutanoate (59). A solution of 2-methylcyclohexanone dimethyl ketal (321 mg, 2.03 mmol) and **1** (477 mg, 2.07 mmol) in 1 mL of methylene chloride was added to a solution of 1.15 mL of $SnCl_4$ in 2 mL of methylene chloride at −78 °C. A solution of benzaldehyde dimethylacetal (305 mg, 2.01 mmol) in 1 mL of methylene chloride was added immediately afterward. After stirring at −40 °C, aqueous workup followed by purification gave 465 mg (70%) of **59** as a mixture of four possible diastereomers: R_f 0.6 (50% methylene chloride in hexane); IR (neat) 1740 (s), 1705 (s); ^1H NMR 0.7–3.3 (m, 19 H, involving a singlet at 3.13), 3.60 (s, 3 H), 3.90 (s, 0.2 H), 4.27 (s, 0.25 H), 4.50 (0.15 H), 4.67 (s, 0.4 H), 7.47 and 7.53 (two singlets with relative intensities of 1:5, 5 H). Anal. ($C_{21}H_{30}O_4$): C, H.

The General Procedure for the Wittig Reaction of Cyclobutanone 2a. (a) With Methyltriphenylphosphonium Bromide and Potassium Hydride.[56] Potassium hydride (22 wt % in mineral oil, 4.0 mol) was freed of the oil by washing with hexane. The phosphonium salt (4.4 mmol) and THF were added and the mixture was heated at 55 °C for 20 min under nitrogen. Cyclobutanone **29** (2 mmol) in 1 mL of THF was added at 0 °C to the yellow reaction mixture, and the mixture was stirred for 3 h at 20 °C. After dilution with hexane, filtration (Hyflosupercell and silica gel), and purification **2b** was obtained. The reaction with the phosphonium fluoroborate was performed similarly.

(b) With Methyltriphenylphosphonium Bromide and Potassium *tert*-Amylate. A mixture of potassium *tert*-amylate (3.30 mmol) and the phosphonium salt (3.50 mmol) in 5 mL of benzene was refluxed for 30 min under nitrogen. A solution of cyclobutanone **2a** (1.0 mmol) in 1 mL of benzene was added to the yellow solution of the ylide, and the mixture was refluxed for 3 h. Workup was performed as above.

Spectral Properties of Methylenecyclobutanes. The methylenecyclobutanes were spectroscopically characterized and used for the subsequent rearrangement.

(56) **Note Added in Proof**: Reproducibility of this procedure with KH from a freshly opened bottle tends to be low, and appears to be improved by addition of a small amount of *tert*-butyl alcohol.

Table X. Wittig Reaction

cyclobutanone			phosphonium salt			potassium base			product		
no.	g	mmol	X^-	g	mmol	B^-	g	mmol	g	% yield	no.
9	0.057	0.205	Br	0.256	0.703	H	0.024	0.586	0.044	78	75d
10	0.102	0.326	Br	0.378	1.06	*t*-AmO	-	0.96	0.077	76	75e
11	0.081	0.278	Br	0.246	0.688	H	0.025	0.626	0.067	83	75c
12	0.308	1.01	Br	0.814	2.28	H	0.083	2.07	0.270	88	75b
13	0.976	3.58	Br	4.33	12.1	*t*-AmO	-	11.0	0.896	90	75a
17	1.11	4.10	Br	3.29	9.03	H	1.50	8.21	0.925	83	60a
19	0.051	0.17	Br	0.372	1.04	*t*-AmO	-	0.95	0.046	90	60b
20	0.304	0.856	BF_4	1.12	3.08	H	0.103	2.57	0.186	67	60c
80a	3.60	11.1	Br	6.86	18.8	H	0.686	17.1	2.86	90	84a

Table XI. TFA Catalyzed Rearrangement of Methylenecyclobutane at Room Temperature

cyclobutane						product			
no.	mg	mmol	TFA, mL	solvent, mL	Rx time, h	no.	mg	% yield	bp(mp), °C, mm Hg
60b	74.4	0.251	0.1	$CDCl_3$, 0.3	0.5	63	39.5	82	-
60c	83.0	0.235	0.1	$CDCl_3$, 0.25	0.5	64	42.1	72	105-110, 0.24
75a	83.0	0.307	0.24	-	1	77a	40.0	80	-
75b	68.0	0.223	0.26	-	1	77b	43.0	97	110-120, 0.30
75c	50.7	0.175	0.40	-	14	77c	27.0	83	(104.5-105.5)
75d	58.0	0.210	0.48	-	14	77d	29.0	81	90-95, 0.50

1-(1-Methoxycyclohexyl)-2-methylene-1-(trimethylsiloxy)cyclobutane (60a): IR (neat) 1240, 1140, 840; ^{1}H NMR 0.10 (s, 9 H), 1.1–2.5 (m, 14 H), 3.25 (s, 3 H, OMe), 4.78 (t, 1 H, J = 1.5 Hz), 4.97 (t, 1 H, J = 2.0 Hz).

1-(1-Methoxycyclooctyl)-2-methylene-1-(trimethylsiloxy)cyclobutane (60b): IR (neat) 1240, 1150, 840; ^{1}H NMR 0.11 (s, 9 H), 1.1–2.5 (m, 18 H), 3.28 (s, 3 H, OMe), 5.01 (t, 1 H, J = 1.5 Hz), 5.20 (t, 1 H, J = 2.0 Hz).

1-(1-Methoxycyclododecanyl)-2-(trimethylsiloxy)cyclobutane (60c): IR (neat) 1250, 840, 1150; ^{1}H NMR 0.13 (s, 9 H), 1.1–2.9 (m, 26 H), 3.23 (s, 3 H, OMe), 4.85 (t, 1 H, J = 1.0 Hz), 5.05 (t, 1 H, J = 1.5 Hz).

1-(1-Methoxy-(*E*)-2-hexenyl)-2-methylene-1-(trimethylsiloxy)cyclobutane (75a): IR (neat) 1660, 1640, 1245, 1150, 970 (m), 885, 840; ^{1}H NMR 0.10 (s, 9 H), 0.8–2.5 (m, 13 H), 3.27 (s, 3 H, OMe), 3.31 and 3.41 (two associated with CC*H*OMe), 4.75 (t, 1 H, J = 2 Hz), 4.91 (t, 1 H, J = 2 Hz), 5.2–5.5 (m, 2 H).

1-(1-Methoxy-3-phenyl-(*E*)-2-propenyl)-2-methylene-1-(trimethylsiloxy)cyclobutane (75b): IR (neat) 1660 (m), 1245, 1150 (s), 970 (m), 875 (m), 840 (s); ^{1}H NMR 0.15 (s, 9 H), 2.0–2.6 (4 H), 3.26 (s, 3 H, OMe), 3.50 (d, 1 H, J = 7 Hz), 4.72 (t, 1 H, J = 2 Hz), 4.91 (t, 1 H, J = 2 Hz), 5.98 (d-d, 1 H, J = 7, 15 Hz), 6.42 (d, 1 H, J = 15 Hz), 7.3 (m, 5 H, C_6H_5).

1-[(4-Methylphenyl)methoxymethyl]-2-methylene-1-(trimethylsiloxy)-cyclobutane (75c): IR (neat) 1250, 1150 (s), 860 (m), 840 (s); ^{1}H NMR 0.210 (s, 9 H), 1.8–2.8 (m, 7 H, involving a singlet at 2.37), 3.43 (s, 3 H, OMe), 4.7–4.9 (m, 2 H, CH_2=), 7.2–7.6 (m, 4 H, aromatic).

1-(Methoxyphenylmethyl)-2-methylene-1-(trimethylsiloxy)cyclobutane (75d): IR (neat) 1670, 1248, 1149 (s), 870 (m), 840 (s); ^{1}H NMR 0.15 (s, 9 H), 1.9–2.8 (m, 4 H), 3.30 (s, 3 H, OMe), 4.09 (s, 1 H), 4.7–5.0 (m, 2 H), 7.1–7.5 (m, 5 H).

1-[(4-Chlorophenyl)methoxymethyl]-2-methylene-1-(trimethylsiloxy)-cyclobutane (75e): IR (neat) 1250, 1150 (s), 840 (s), 830 (m); ^{1}H NMR 0.09 (s, 6.3 H), 0.11 (s, 2.7 H), 1.9–2.5 (m, 4 H), 3.23 (s, 3 H, OMe), 3.93 (s, 0.7 H), 3.97 (s, 0.3 H), 4.6–4.8 (m, 2 H), 7.19 (s, 4 H, aromatic).

1-(*c*-4-*tert*-Butyl-*r*-1-methoxycyclohexyl)-2-methylene-1-(trimethylsiloxy)cyclobutane (84): IR (neat) 1260, 1150, 895, 840; ^{1}H NMR 0.13 (s, 9 H), 0.8–2.5 (m, 19 H, involving a singlet at 0.85), 3.20 (s, 3 H), 4.73 (t, 1 H, J = 2 Hz), 4.92 (t, 1 H, J = 2 Hz).

4-Methylenespiro[4.5]decan-1-one by the Rearrangement of 60. (a) With BF_3 as Catalyst. The cyclobutane **60a** (358 mg, 1.33 mmol) in 2 mL of methylene chloride was treated with 0.16 mL of BF_3·Et_2O (1.33 mmol) at room temperature for 1 h. Ether was added and the organic phase was washed with saturated $NaHCO_3$ and saturated NaCl. Drying, concentration, and purification gave 187 mg of a product mixture. A 161-mg portion of the crude product was further purified by medium pressure chromatography (Lobar column, Grosse A, 2% ethyl acetate in hexane) to give a mixture of **61** and its isomer **62**.

4-Methylenespiro[4.5]decan-1-one (61): 82.6 mg (53%); R_f 0.47 (5% ethyl acetate in hexane, two developments); GLC retention time, 6.1 min (column A, 100 °C); IR (neat) 1730 (s, C=O), 1635, 880 (m, C=C); ^{1}H NMR 1.1–2.9 (m, 14 H), 4.92 (m, 2 H); MS, m/e (rel intensity) 164 (M^+, 19), 136 (100), 122 (25), 107 (59), 93 (47), 81 (45), 79 (90), 77 (27), 67 (40), 41 (40), 39 (36), 28 (26). Anal. ($C_{11}H_{16}O$): C, H.

2-Methylenespiro[4.5]decan-1-one (62): 36.2 mg (29%) F_f 0.51; GLC retention time, 7.0 min; IR (neat) 1713 (s, C=O), 1628 (m); ^{1}H NMR 1.0–2.0 (m, 12 H, involving a triplet at 1.74), 2.3–2.7 (m, 2 H), 5.05–5.25 (m, 1 H), 5.70–5.90 (m, 1 H). This compound was unstable, and reasonable analtical data could not be obtained.

(b) General Procedure with TFA. TFA (92.9 μL, 1.21 mmol) was added at 0 °C to a solution of cyclobutane **60a** (64.7 mg, 0.241 mmol) in 0.25 mL of 2,2,2-trifluoroethanol. After 35 min at room temperature, the mixture was diluted with ether, washed with aqueous $NaHCO_3$ and saturated NaCl, dried, and concentrated. The crude product was purified to give ketone **61** as a single isomer (32.1 mg, 81%). The reaction with TfOH was carried out similarly. The reaction of **75a–e** was performed in TFA as solvent.

2-(4-Chlorophenyl)-3-methyl-2-cyclopenten-1-one (77e). TFA (0.49 ml) was added to **20e** (51 mg, 0.213 mmol) placed in an NMR tube at 35 °C, and the reaction was monitored by NMR. The formation of **21e** was initially observed (δ 4.0–4.2, 1 H, CH=) and then **22e** gradually formed (MeOH at δ 3.13 was taken as a standard). After 15 h, the title compound was isolated by chromatography (32 mg, 90%): IR (neat) 1690 (s), 830 (m); ^{1}H NMR 2.0–2.7 (m, 7 H, involving a singlet at 2.14), 7.0–7.4 (m, 4 H, aromatic). An analytical sample was obtained as a 2,4-DNP derivative: mp 241.0–241.5 °C (aqueous EtOH). Anal. ($C_{18}H_{15}O_4N_4Cl$): C, H.

Spectral Properties of Cyclopentanones. 4-Methylenespiro[4.7]dodecan-1-one (63): bp 90–95 °C (bath temperature) (0.07 mm); IR (neat) 1715 (s), 1630, 880 m); ^{1}H NMR 1.2–2.8 (m, 18 H), 4.85 (t, J = 1.5 Hz), 4.98 (t, J = 2 Hz); MS, m/e (relative intensity) 192 (M^+, 39), 164 (16), 136 (33), 135 (30), 110 (660, 109 (91), 107 (41), 96 (40), 95 (40), 93 (58), 81 (79), 79 (92), 67 (100), 55 (71), 41 (90). Anal. ($C_{13}H_{20}O$); C, H.

4-Methylenespiro[4.11]hexadecan-1-one (64): bp 105 °C (0.24 mm); IR (neat) 1705 (s, C=O), 1635, 880 (m); ^{1}H NMR 1.1–2.8 (m, 26 H), 4.7–5.0 (m, 2 H, CH_2=); MS, m/e (relative intensity) 248 (M^+, 41), 122 (47), 109 (93), 108 (770), 95 (57), 94 (49), 83 (61), 82 (44), 81 (64), 79 (58), 67 (58), 55 (75), 41 (100). Anal. ($C_{17}H_{28}O$): C, H.

4-Methylspiro[4.7]dodec-3-en-1-one (65): IR (neat) 1730 (s, C=O); ^{1}H NMR 1.2–1.9 (m, 17 H, involving a multiplet at 1.7–1.9, Me), 2.6–2.8 (m, 2 H, CH_2C=), 5.4–5.6 (m, 1 H, CH=); MS, m/e (relative intensity) 192 (M^+, 56), 164 (14), 149 (28), 136 (36), 135 (22), 121 (22), 109 (72), 96 (39) 93 (36), 81 (55), 79 (55), 67 (50), 55 (36), 40 (100).

3-Methyl-2-(*trans*-1-pentenyl)-2-cyclopenten-1-one (77a): IR (neat) 1680 (s), 1585 (m); ^{1}H NMR 0.8–1.1 (distorted t, 3 H), 1.2–2.7 (m, 11 H, involving a singlet at 2.10), 5.93 (d, 1 H, J = 16 Hz), 6.3–7.0 (dt, 1 H, J = 7, 16 Hz); MS m/e (relative intensity) 164 (M^+, 100), 149 (60), 135 (59), 131 (25), 122 (62), 110 (48), 107 (28), 93 (51), 91 (53), 79 (44), 55 (28).

3-Methyl-2-(2-phenylethenyl)-2-cyclopenten-1-one (77b): mp 74.5–75.5 °C; IR (neat) 1680 (s), 975 (s), 755, 690 (s); ^{1}H NMR 2.0–2.6 (m, 7 H, involving a singlet at 2.10), 6.61 (d, 1 H, J = 16 Hz), 7.0–7.8 (m, 6 H, involving a doublet, J = 16 Hz at 7.55). Anal. ($C_{14}H_{14}O$): C, H.

3-Methyl-2-(4-methylphenyl)-2-cyclopenten-1-one (77c): mp 104.5–105.5 °C (hexane) (lit.[31b] mp 108–109 °C); IR (neat) 1680 (s);

^{1}H NMR 2.14 (s, 3 H), 2.2–2.7 (m, 7 H, involving a singlet at 2.33), 7.03 (s, 4 H, aromatic); MS *m/e* (relative intensity) 186 (M^+, 100), 143 (81), 128 (67), 115 (65).

2-Phenyl-3-methyl-2-cyclopenten-1-one (77d): bp 90–95 °C (0.5 mm); IR (neat) 1690 (s), 1630 (m), 765, 700 (m); ^{1}H NMR 2.15 (s, 3 H), 2.3–2.75 (m, 4 H), 7.17 (s, 5 H, C_6H_5); MS, *m/e* (relative intensity) 172 (M^+, 98), 129 (100), 115 (63). Anal. ($C_{12}H_{12}O$): C, H.

(*Z*)-1-(1-Methoxycyclohexyl)-2-ethylidene-1-(trimethylsiloxy)cyclobutane (66). The cyclobutanone **16** (924 mg, 3.42 mmol) was treated with the ylide generated from 4.63 g of the phosphonium bromide (12.5 mmol) and potassium hydride (417 mg, 10.4 mmol) to obtain 609 mg (69%) of **66** (*E*:*Z* = 8:92) after chromatography (Lobar, Grosse B): GLC retention time 4.9 min for the *E* isomer and 6.0 min for the *Z* isomer (column B, 170 °C); IR (neat) 1240, 1175 (s), 835 (s); ^{1}H NMR 0.13 (s, 9 H), 0.7–2.4 (m, 17 H, involving a broad triplet at 1.70), 3.27 (s, 0.24 H, OMe of the *E* isomer), 3.28 (s, 2.76 H, OMe of the *Z* isomer), 5.06 (br q, 1 H, *J* = 7 Hz). Anal. ($C_{16}H_{30}O_2Si$): C, H.

(*Z*)-4-Ethylidenespiro[4.5]-1-decanone (67). TFA (112 μL, 1.46 mmol) was added at 0 °C to **66** (82.2 mg, 0.291 mmol) in 0.3 mL of methylene chloride. The mixture was worked up after 1 h, and the crude product was purified to obtain 34.3 mg of **67** (66%) as a 2:98 mixture of *E* and *Z* isomers: bp 85–90 °C (2.7 mm); GLC retention times, 9.0 min for *Z* and 9.5 min for *E* (column A, 140 °C); IR (neat) 1710 (s), 815 (m); ^{1}H NMR 1.1–2.6 (m, 17 H, involving a broad triplet at 1.76, *J* = 7 Hz), 5.37 (br q, 1 H, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$) 13.98 (Me), 21.64, 25.56, 29.19 (C-3), 31.24, 37.38, 50.20 (C-5), 119.0 (=*C*HMe), 144.8 (C-4), 222.1 (C-1). Anal. ($C_{12}H_{18}O$): C, H.

(*E*)-4-Ethylidenespiro[4.5]-1-decanone (68). The *Z* isomer **67** (20.0 mg, 0.112 mmol) was dissolved in 50 μL of benzene containing 0.5 mol % of azobisisobutyronitrile (AIBN) and thiophenol (11.5 μL, 0.224 mmol) and heated at 65 °C for 5 h. The mixture was diluted with ether, washed twice with 2 M NaOH solution, dried, and concentrated. Chromatographic purification gave 12.5 mg of **68** (63%) as a 97:3 mixture of *E* and *Z* isomers: IR (neat) 1725 (s); ^{1}H NMR 1.1–2.6 (m, 17 H, involving a broad triplet at 1.68, *J* = 7 Hz), 5.35 (br q, 1 H, *J* 7 Hz); ^{13}C NMR ($CDCl_3$) 13.63 (Me), 21.70, 22.23 (C-3), 25.68, 31.24, 33.22, 25.92, 51.83 (C-5), 116.9 (=*C*Me), 145.7 (C-4). Anal. ($C_{12}H_{18}O$): C, H.

(*Z*)-3-Ethylidene-2-methyl-2-(3-butenyl)cyclopentanone (71). A mixture of 5-hexen-2-one dimethyl ketal (**69**) (5.10 g, 35.3 mmol) and **1** (8.60 g, 37.0 mmol) in 50 mL of methylene chloride was added to a solution of BF_3·Et_2O (4.55 mL) in 35 mL of methylene chloride at −78 °C. After 10 min, the mixture was worked up as usual to give 9.00 g of the adduct, pure by TLC: IR (neat) 1765 (s), 1625 (m), 1245, 1160 (s), 840 (s); ^{1}H NMR 0.15, 0.18 (s, 9 H), 1.14, 1.17 (s, 3 H), 1.4–2.9 (m, 8 H), 3.14 (s, 1.6 H, OMe), 3.17 (s, 1.4 H, OMe), 4.6–5.2 (m, 2 H, $=CH_2$), 5.3–6.1 (m, 1 H, CH=).

The adduct (2.54 g, 9.40 mmol) was treated with the ethylidene ylide generated from the phosphonium bromide (12.6 g, 34.0 mmol) and potassium hydride (1.13 g, 28.8 mmol) in THF to obtain crude **70** (3.02 g): IR (neat) 1620 (m), 1240, 840; ^{1}H NMR 0.13 (s, 9 H), 0.5–2.9 (m, 14 H, involving a singlet at 1.20, and a broad triplet at 1.70), 3.25 (s, 1.5 H, OMe), 3.28 (s, 1.5 H, OMe), 4.7–6.0 (m, 4 H).

The crude **70** (565 mg, 2.00 mmol) in 2 mL of methylene chloride was treated wtih TFA (0.11 mL) for 1 h. After the usual workup and purification 160 mg of **71** was obtained (46% from the ketal). The yield of this rearrangement as determined in a duplicate run was 75%: IR (neat) 1710 (s), 1630 (m); ^{1}H NMR 1.13 (s, 3 H), 1.4–2.8 (m, 11 H, involving a broad triplet at 1.75, *J* = 7 Hz), 4.6–5.1 (m, 2 H), 5.2–5.7 (m, 2 H). Anal. ($C_{12}H_{18}O$): C, H.

1-(*Z*)-Ethylidene-7a-methyl-2,3,7,7a-tetrahydro-5(6*H*)-indanone (73). A suspension of cuprous chloride (55.5 mg, 0.561 mmol) and palladium chloride (19.9 mg) in 0.4 mL of DMF was stirred under oxygen for 1 h; **71** (79.7 mg, 0.447 mmol) in 0.1 ml of DMF was added to the suspension and over 14 h to give **72** (55.6 mg, 64%) after purification: GLC retention time, 4.6 min (column A, 160 °C), ca. 90% isomerically pure; IR (neat) 1735, 1710; ^{1}H NMR 1.22 (s, 3 H), 1.5–2.8 (m, 14 H, involving a broad doublet at 1.72, *J* = 7 Hz), 5.2–5.7 (broad q, 1 H, *J* = 7 Hz).

A mixture of **72** (45.4 mg, 0.234 mmol), β-alanine (41.6 mg, 0.467 mmol), toluene (0.8 mL), and acetic acid (0.2 mL) was refluxed for 5 h, at which point the starting material had been consumed. Filtration and purification gave **73** (12.0 mg, 29%): IR (neat) 1658 (m), 1649 (sh); ^{1}H NMR 1.38 (s, 3 H), 1.4–2.5 (m, involving a broad doublet at 1.70, *J* =), 5.30 (br q, 1 H, *J* = 7 Hz), 6.55–6.65 (m, 1 H); MS *m/e* (relative intensity) 176 (M^+, 69), 148 (58), 133 (100), 134 (64), 119 (51), 105 (77), 91 (71), 77 (43), 55 (36), 43 (47).

4-(*c*-4-*tert*-Butyl-*r*-methoxycyclohexyl)-4-oxobutanoic Acid (81a). Oxidation of the crude cyclobutanone **80a** with 2.5 equiv of basic hydrogen peroxide gave the title acid as white crystals, homogeneous by ^{13}C NMR and TLC, mp 109.0–111.5 °C (894 mg, 87% from 79a). Recrystallization from hexane gave an analytical sample: mp 113.0–114.0 °C; IR (neat) 3500–2400 (br), 1710 (br); ^{1}H NMR 0.90 (s, 9 H), 1.0–2.2 (m, 9 H), 2.4–2.9 (A_2B_2m, 4 H), 3.12 (s, 3 H), 10.19 (s, 1 H); ^{13}C NMR ($CDCl_3$) 21.90, 27.53 (*tert*-butyl), 27.71, 30.88, 31.00, 32.41 (*tert*-butyl), 47.20 (*c*-4), 51.84 (OMe), 82.72 (*C*–O), 178.7, 213.4. Anal. ($C_{15}H_{26}O_4$): C, H.

Methyl 4-(*c*-4-*tert*-butyl-*r*-1-hydroxycyclohexyl)-4-oxobutanoate (82). The cyclobutanone **80b** obtained in the usual manner was oxidized (to **81b**) and then esterified: ^{1}H NMR 0.84 (s, 9 H), 1.0–3.0 (m, 13 H), 3.57 (s, 3 H), 4.23 (s, 2 H), 7.0–7.4 (m, 5 H).

The benzyl group was removed by hydrogenolysis over 5% Pd/C in acetic acid/ethanol to give the title ester, which was identical with an authentic sample of the axial alcohol prepared as described below.

The Preparation of Authentic 82 and 83. To a solution of **46** in 1.5 mL of methylene chloride was added solid $NaHCO_3$ (259 mg, 3.1 mmol) and then *m*-chloroperbenzoic acid (313 mg of 85% pure material). After 2 h the mixture was worked up and the crude silyl ether (286 mg) was treated with potassium fluoride in methanol. Chromatographic purification gave 109 mg of **82** and 68 mg of **83** (62:38 ratio, 66%).

The Axial Alcohol 82: mp 65.5–66.0 °C (plates from hexane); R_f 0.52 (30% ethyl acetate in hexane); GLC retention time, 11.4 min (column A, 180 °C); IR (0.04 M CCl_4) 3470 (vw, OH), 1737 (vs), 1700 (vs); ^{1}H NMR 1.06 (s, 9 H), 1.1–2.9 (m, 13 H, involving A_2B_2m at 2.3–2.9, 3.1–3.3 (m, 1 H), 3.58 (s, 3 H); MS, *m/e* (rel) 270 (M^+, 0.6, 154 (41), 114 (14), 94 (25), 81 (50), 69 (24), 67 (29), 59 (24), 57 (100), 55 (75), 43 (53), 41 (80). Anal. ($C_{12}H_{20}O_4$): C, H.

The Equatorial Alcohol 83: mp 74.5–75.0 °C (fine needles from hexane); R_f 0.36; IR (0.04 M CCl_4) 3600–3300, 1735, 1712; ^{1}H NMR 0.89 (s, 9 H), 0.9–3.0 d(m, 14 H, involving A_2B_2m at 2.3–3.0), 3.59 (s, 3 H); MS, *m/e* (relative intensity) 270 d(M^+, 3), 252 (16), 221 (10), 154 (89), 136 (20), 114 (22), 94 (30), 81 (58), 69 (30), 67 (34), 59 (20), 57 (100), 55 (56), 43 (45), 41 (47). Anal. ($C_{12}H_{20}O_4$): C, H.

***c*-8-*tert*-Butyl-4-methylene-*r*-spiro[4.5]decan-1-one (85).** TFA (3.15 mg, 41 mmol) was added to a solution of **84** (2.55 g, 8.19 mmol) at 0 °C and the mixture was worked up after 1 h. GLC analysis of the crude product indicated a 94:6 ratio of **85** and its 2-methylene isomer **86**. Chromatographic purification (50 g silica gel) gave 1.32 g of the product. A portion (580 mg) of the product was further purified by MPLC (Lobar, Grosse B, 1% ethyl acetate in hexane) to obtain 345 mg of **85** (50% yield) and 33 mg of **86** (5%), which was not stable enough for elemental analysis.

85: mp 46.8–47.2 °C; R_f 0.55 (5% ethyl acetate in hexane, developed twice); GLC retention time, 8.3 min (column A, 160 °C); IR (neat) 1725 (s), 1650, 880 (s); ^{1}H NMR 0.7–2.8 (m, 19 H, involving a singlet at 0.90), 4.71 (t, 1 H, *J* = 1 Hz), 4.82 (t, 1 H, *J* = 2 Hz); ^{13}C NMR ($CDCl_3$) 22.41, 27.03, 27.50 (*tert*-butyl), 32.41, 33.99, 36.40, 47.62, 50.78 (C-5), 106.13 (CH_2=), 155.50 (C-4), 219.70; MS, *m/e* (relative intensity) 192 (M^+ − 28, 1.6), 135 (11), 79 (11), 69 (10), 57 (100), 55 (37), 53 (30), 41 (92). Anal. ($C_{15}H_{24}O$): C, H.

86: R_f 0.64; GLC retention time, 7.9 min; IR (neat) 1708 (s), 1702 nsh), 1625; ^{1}H NMR 0.9–2.0 (m, 19 H, involving a singlet at 0.92), 5.9–6.1 (m, 1 H), 7.0–7.2 (m, 1 H).

4-Acetoxy-*t*-8-*tert*-butyl-*r*-1-spiro[4.5]decan-1-one (87). The crude **85** (140 mg, 0.639 mmol) was reduced with LAH (58 mg, 1.37 mmol) in ether to obtain 133 mg of the alcohol. A 130-mg portion of the product was acetylated (acetic anhydride and 4-(dimethylamino)-pyridine) to give *c*-8-*tert*-butyl-4-methylene-*r*-1-spiro[4.5]decanyl acetate (154 mg): IR (neat) 1732; ^{1}H NMR 0.7–2.6 (m, 25 H, involving a singlet at 0.84 and 1.93), 4.5–4.8 (m, 2 H), 5.0–5.2 (m, 1 H).

The acetate (42.5 mg) was ozonized to give **87** (24 mg, 53% from **85**). This material was clearly different from the isomeric **88** by GLC and TLC; the retention times of 10.0 and 10.7 min (column A, 170 °C) and the R_f values of 0.29 and 0.33 (10% ethyl acetate in hexane, developed twice) were recorded for **87** and **88** respectively. Spectral properties are as follows: IR (neat) 1730; ^{1}H NMR 0.8–2.4 (m, 25 H, involving singlets at 0.85 and 1.97), 5.2–5.4 (m, 1 H); MS, *m/e* (20 eV, relative intensity) 266 (M^+, 12), 223 (40), 206 (70), 167 (41), 150 (100), 149 (84), 122 (34), 109 (32), 108 (44), 57 (56).

***c*-7-Methyl-4-methylene-*r*-1-spiro[4.5]decan-1-one (91).** A mixture of 3-methylcyclohexanone dimethyl ketal (1.22 g, 7.00 mmol) and **1** (1.79 g, 7.70 mmol) was treated with 0.43 mL of BF_3·Et_2O in 17 mL of methylene chloride at −78 °C for 20 min to obtain **90** as a ca. 1:1 mixture of isomers (2.15 g): IR (neat) 1778 (s), 1245, 1170, 845 (s); ^{1}H NMR 0.06 (s, 9 H), 0.7–2.9 (m, 16 H, involving doublets at 0.79 and 0.838 *J* = 7 Hz, of equal intensity), 3.12 (s, 3 H).

The crude **90** was treated by the ylide generated from the methylphosphonium bromide (1.54 g, 4.23 mmol) and potassium hydride (141 mg, 3.52 mmol) to obtain 452 mg of the methylene cyclobutane (97% from the ketal): IR (neat) 1255, 1145, 840; ^{1}H NMR 0.12 (s, 9 H), 0.9–2.6 (m, 16 H, involving a doublet at 0.87, *J* = 6.5 Hz), 3.19 (s, 3

H), 4.40 (t, 1 H, J = 2 Hz), 4.59 (t, 1 H, J = 2 Hz).

TFA (0.28 mL) was added to a solution of the cyclobutane (204 mg, 0.716 mmol) in trifluoroethanol (0.8 mL) and the mixture was stirred for 2 h at room temperature. Purification by MPLC (Lobar, Grosse B) gave 70 mg of **91** (54%) and its isomer **92** (11 mg, 10%), which was not stable enough to obtain good analytical data.

91: bp 85–90 °C (0.08 mm); R_f 0.45 (3% ethyl acetate in hexane, developed twice); IR (neat) 1720, 1655, 885: ^{1}H NMR 0.8–2.9 (m, 16 H, involving a doublet at 0.87, J = 7 Hz), 4.77 (t, 1 H, J = 7 Hz), 4.86 (t, 1 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) 21.59 (Me), 22.76, 27.09, 33.29, 34.52, 36.56, 41.65 (Me*C*), 52.07 (C-5), 106.30 (CH_2=), 155.73 (C=), 220.32; MS, *m/e* (relative intensity) 178 (M^+, 12), 150 (100), 110 (67), 109 (52), 108 (42), 96 (80), 94 (64), 81 (60), 79 (69), 69 (44), 55 (53), 41 (77). Anal. ($C_{12}H_{18}O$): C, H.

92: R_f 0.50; IR (neat) 1720 (s), 1630; UV (0.202 mM in ethanol), λ_{max} 230 nm (log ϵ_{max} 3.70); ^{1}H NMR 0.7–2.9 (m, 16 H, involving a doublet at 0.85, J = 7 Hz), 5.10 (m, 1 H), 5.80 (m, 1 H); MS, *m/e* (relative intensity), 178 (M^+, 30), 150 (24), 137 (100), 95 (58), 91 (30), 80 (36), 78 (35).

4-(*c*-3-Methyl-*r*-methoxycyclohexyl)-4-oxobutanoic Acid (93). The crude **90** (210 mg, 0.733 mmol) was treated with excess basic hydrogen peroxide to give the title acid (143 mg, 81% from the ketal): mp 52.5–53.5 °C (hexane); ^{1}H NMR 0.8–3.0 (m, 1. H, involving a doublet at 0.90, J = 7 Hz, and A_2B_2m at 2.3–3.0), 3.14 (s, 3 H), 10.0 (br, 1 H); ^{1C} NMR ($CDCl_3$) 20.89, 22.41, 27.20, 27.67, 29.71, 30.89, 34.11, 38.79, 51.89, 83.83, 178.73, 213.42. Anal. ($C_{12}H_{20}O_4$): C, H.

The Aldol Reaction of 1 and 2-Methylcyclohexanone Dimethyl Ketal. A mixture of the ketal (1.10 g, 7.00 mmol) and **1** (1.71 g, 7.70 mmol) was treated with BF_3·Et_2O (0.43 mL, 3.50 mmol) in 15 mL of methylene chloride at −78 °C for 20 min to obtain **94** (1.71 g, 86%) and **95** (173 mg, 8%).

94: R_f 0.40 (5% ethyl acetate in hexane, developed twice); IR (neat) 1770 (s), 1245, 1140, 840; ^{1}H NMR 0.07 (s, 8 H), 0.09 (s, 1 H), 0.6–3.0 (m, 16 H, involving a doublet at 0.76, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) 1.52, 16.44 (Me × 0.9), 16.73 (Me × 0.1), 22.23, 25.78, 26.20, 26.38, 31.12, 36.87 (*C*Me), 42.70, 51.54 (MeO), 80.67 (MeO*C*), 97.82 (Me_3SiOC), 215.17.

95: F_f 0.34 and 0.29; IR (neat) 1775, 1250, 840; ^{1}H NMR 0.13 (s, 9 H), 0.8–3.0 (16 H, involving a doublet at 0.93, J = 6.8 Hz), 3.17 (s, 3 H); ^{13}C NMR ($CDCl_3$) 1.46, 14.74 (Me × 0.2), 15.79 (Me × 0.8), 19.48, 21.29, 21.82, 24.39, 25.33, 27.32, 27.96, 28.19, 28.66, 28.84, 29.60, 30.48, 41.42, 41.65, 42.00, 50.08 (OMe × 0.8), 51.48 (*O*Me × 0.2), 76.17 (MeO*C* × 0.2), 79.33 (MeO*C* × 0.2), 98.87 (TMSO*C* × 0.2), 100.27 (TMSO*C* × 0.8), 210.08 (C=O × 0.2), 210.43 (C=O × 0.8).

4-(*c*-2-Methyl-*r*-1-methoxycyclohexyl)-4-oxobutanoic Acid (96). The ketone **94** (187 mg, 0.653 mmol) was treated with basic hydrogen peroxide to obtain **96** (83.8 mg, 53%): mp 94.5–95.0 °C (fine plates from hexane); IR (0.04 M CCl_4) 3500–2600, 1710 (sh), 1700 (vs); ^{1}H NMR 0.7–3.0 (m, 19 H, involving a doublet, J = 6.5 Hz, and A_2B_2m at 2.3–2.9), 3.21 (s, 3 H), 11.6 (br, 1 H). Anal. ($C_{12}H_{20}O_4$): C, H.

4-(*t*-2-Methyl-*r*-1-methoxycyclohexyl)-4-oxobutanoic Acid (97). The ketone **95** (33.0 mg, 0.115 mmol) was oxidized to obtain **97** (20.4 mg, 71%): mp 86.0–87.0 °C (needles from hexane); IR (0.04 M CCl_4) 3500–2600, 1703; ^{1}H NMR 0.7–2.9 (m, 1. H, involving a doublet at 0.76, J = 6.5 Hz, and A_2B_2m at 2.3–2.9), 3.09 (s, 3 H, OMe), 11.02 (s, 1 H). Anal. ($C_{12}H_{20}O_4$): C, H.

***c*-6-Methyl-4-methylene-*r*-1-spiro[4.5]decan-1-one (98).** The ketone **94** (300 mg, 1.05 mmol) was treated with the ylide from methylphosphonium bromide (1.00 g, 2.75 mmol) and potassium hydride (100 mg, 2.05 mmol) to obtain the methylenecyclobutane (169 mg, 57%): ^{1}H NMR 0.12 ns, 9 H), 0.7–3.0 (m, 16 H, involving a doublet at 0.79, J = 6.5 Hz), 3.26 (s, 3 H, OMe), 4.81 (t, 1 H, J = 2 Hz), 5.01 (t, 1 H, J = 2.5 Hz).

A solution of this product (73 mg, 0.257 mmol) in 0.26 mL of methylene chloride was treated with 0.1 mL of TFA for 1.5 h to obtain, after MPLC purification, 23.1 mg of **98**, which was clearly distinguishable by GLC from the isomeric **99**: GLC retention time 4.8 min (column A, 150 °C); bp 85–90 °C (bath temperature) (0.07 mm); IR (neat) 1710 (s), 1635, 890 (m); ^{1}H NMR 0.6–3.0 (m, 16 H, involving a doublet at 0.75, J = 6 Hz), 4.80 (t, 1 H, J 2 Hz), 4.97 (t, 1 H, J = 2 Hz); MS, *m/e* (relative intensity) 178 (30), 163 (52), 150 (100), 136 (100), 135 (60), 113 (45), 112 (60), 111 (55), 110 (98), 109 (80), 95 (90), 93 (95), 91 (70), 81 (74), 79 (95), 77 (70), 67 (90), 55 (80), 53 (60), 41 (90), 39 (80).

The reaction mixture also contained small amounts of a relatively unstable, isomeric UV-active component, which was tentatively assigned as the 2-methylenespirodecan-1-one.

When the above transformation was performed on a 9:1 mixture of the ketones **94** and **95** (ca. 45% yield), a mixture of **98** and **99** was obtained in a ratio of ca. 9:1.

***t*-6-Methyl-4-methylene-*r*-1-spiro[4.5]decan-1-one (99).** The ketone **95** (100 mg, 0.35 mmol) was treatred with the ylide generated from methylphosphonium bromide (275 mg, 0.754 mmol) and potassium hydride (27.5 mg, 0.67 mmol) to obtain 1-(*t*-2-methyl-*r*-methoxycyclohexyl)-2-methylene-1-(trimethylsiloxy)butane (50 mg, 51%): ^{1}H NMR 0.13 (s, 9 H), 0.7–3.0 (m, 16 H, involving a doublet at 0.90, J 7 Hz), 3.27 (s, 2.1 H), 3.57 (s, 0.9 H), 4.88 (t, 1 H, J = 2 Hz), 5.11 (t, 1 H, J = 2 Hz).

This material (24.3 mg, 0.085 mmol) was treated with 33 μL of TFA at 20 °C for 1 min to give after purification the title compound (9.1 mg, 22%) free from the isomeric **98**: IR (neat) 1715, 640; ^{1}H NMR 0.6–2.9 (m), 5.0–5.2 (m, olefinic protons); MS *m/e* (relative intensity) 178 (M^+, 50), 163 (40), 150 (42), 136 (100), 135 (39), 122 (40), 121 (40), 110 (95), 95 (80), 93 (90), 79 (90), 67 (65), 55 (58), 53 (50), 41 (82), 39 (65).

4-Acetoxy-*c*-8-*tert*-1-spiro[4.5]decan-1-one (88). The crude **80a** (435 mg, 1.28 mmol) was reduced with excess LAH in ether to obtain the corresponding alcohol (400 mg). A 380-mg portion of this was trimethylsilylated to give **100** (418 mg, 71% from **79a**): IR (neat) 1255, 840; ^{1}H NMR 0.12 (s, 9 H), 0.16 (s, 9 H), 0.7–2.3 (m, 22 H, involving a singlet at 0.86), 3.24 (s, 3 H), 3.9–4.3 (m, 1 H).

The cyclobutane **100** (201 mg, 0.501 mmol) in 1 mL of methylene chloride was treated with $SnCl_4$ (59 μL, 0.501 mmol) initially at −70 °C and then at 0 °C for 15 min to give, after acetylation of the hydroxyl group at C-4, the title compound. GLC comparison of this crude acetate with authentic samples showed a 62:1 ratio of **88** and **87**. Chromatographic purification gave 98 mg of **88** (76% from the ketal), which was identical with a sample prepared from **89** by TLC, GLC, ^{1}H NMR and MS: bp 110 °C (bath temperature) (2 mm); mp 63.0–63.5 °C; GLC retention times, 10.0 and 10.7 min for **87** and **88**, respectively (column A, 170 °C); IR (0.05 M CCl_4) 1730 (vs); ^{1}H NMR 0.8–2.4 (m, 25 H, involving singlets at 0.85 and 1.97), 4.7–4.9 (m, 1 H); MS *m/e* (relative intensity) 266 (M^+, 15), 206 (90), 167 (18), 150 (100), 149 (55), 122 (56), 109 (79), 108 (80). Anal. ($C_{16}H_{26}O_3$): C, H.

Preparation of 88 from 89. The spiro ketone **89**[37] (11.4 mg, 0.0055 mmol), *N*-bromosuccimide (10.8 mg, 0.061 mmol), and 1 mg of AIBN in CCl_4 (0.4 ml) were refluxed to give 17.3 mg of crude 4-bromo-*c*-8-*tert*-butylspiro[4.5]dec-2-en-1-one: ^{1}H NMR 0.9–2.2 (m, 18 H, involving a singlet at 1.05), 4.7–4.9 (m, 1 H), 6.00 (dd, 1 H, J = 1.8, 7.0 Hz), 7.42 (dd, 2.5, 7.0 Hz).

The crude bromide (16.3 mg) was treated with 11.1 mg of silver acetate in acetic acid (15 μl) and acetic anhydride (15 μl) at 130 °C for 3 h to give the corresponding 4-acetoxy compound (5.0 mg): ^{1}H NMR 0.7–2.2 (m, 21 H, involving singlets at 0.88 and 2.01), 5.2–5.4 (m, 1 H), 5.9–6.1 (m, 1 H), 7.12 (dd, 1 H, J = 2.5, 6.0 Hz).

The acetate was hydrogenated over 5% Rh on alumina in ethanol to give the title compound (4.3 mg). This compound was identical with the sample of **88** prepared by the rearrangement reaction (vide supra).

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Registry No. **45**, 65213-31-2; **46**, 65268-62-4; **47**, 88441-46-7; **48**, 65213-32-3; **49**, 65213-33-4; **50**, 65213-34-5; **51**, 88441-47-8; (±)-**52**, 88441-48-9; (±)-**53**, 88441-49-0; (±)-**54**, 88441-50-3; (±)-**55**, 88494-67-1; **57**, 65213-37-8; **58**, 65213-39-0; **59** (isomer 1), 88441-51-4; **59** (isomer 2), 88494-68-2; **59** (isomer 3), 88494-72-8; **59** (isomer 4), 88494-73-9; **60a**, 88441-52-5; **60b**, 88441-53-6; **60c**, 88441-54-7; **1**, 17082-61-0; **6**, 62248-59-3; **7**, 62248-60-6; **8** (isomer 1), 88441-28-5; **8** (isomer 2), 88441-29-6; **9**, 87505-92-8; **10**, 87505-93-9; **11**, 87505-91-7; **12**, 87505-90-6; **13**, 87505-89-3; **14**, 69152-11-0; **15**, 88441-30-9; **16**, 62276-31-7; **17**, 69152-08-5; **18**, 69152-09-6; **19**, 88441-31-0; **20**, 88441-32-1; **21**, 88441-33-2; **22**, 88441-34-3; **23**, 5864-79-9; **24**, 88441-35-4; **25**, 88441-36-5; **26**, 62248-57-1; **27**, 39984-92-4; **28**, 62248-56-0; **29**, 88441-37-6; **30**, 88441-38-7; **31**, 62248-58-2; **32**, 62248-61-7; **34**, 88441-39-8; **35**, 88441-40-1; **36**, 88441-97-8; **37**, 88441-41-2; **38**, 88441-42-3; **39**, 88441-43-4; **40**, 88441-44-5; **41**, 88441-45-6; **42**, 65213-30-1; **43**, 54966-52-8; **44**, 65213-35-6; **61**, 88441-55-8; **62**, 88441-56-9; **63**, 88441-57-0; **64**, 88441-58-1; **65**, 88441-59-2; **66**, 88441-60-5; **67**, 88453-19-4; **68**, 88441-61-6; **69**, 88441-62-7; **70**, 88441-63-8; **70** (ketone), 88441-91-2; **71**, 88441-64-9; **72**, 88441-65-0; **73**, 88441-66-1; **75a**, 87505-94-0; **75b**, 87505-95-1; **75c**, 87505-96-2; **75d**, 87505-97-3; **75e**, 87505-98-4; **76e**, 88441-67-2; **77a**, 87506-04-5; **77b**, 88441-68-3; **77c**, 70855-14-0; **77d**, 50397-92-7; **77e**, 87506-06-7; **79a**, 944-19-4; **79b**, 88278-94-8; **80a**, 88441-69-4; **80b**, 88441-70-7; **81a**, 88441-71-8; **81b**, 88441-72-9; **82**, 88441-73-0; **83**, 88441-74-1; **84**, 88441-75-2; **85**, 88441-76-3; **85**-ol (acetate), 88441-92-3; **86**, 88441-77-4; **87**, 88441-78-5; **88**, 88441-79-6; **89**, 87506-17-0; **89** (4-bromo deriv.), 88441-94-5; **89** (4-acetate), 88441-95-6; **90** (isomer 1), 88441-80-9; **90**

(isomer 2), 88441-98-9; **91**, 88441-81-0; **92**, 88441-82-1; **93**, 88441-83-2; **94** (isomer 1), 88441-84-3; **94** (isomer 2), 88494-69-3; **95** (isomer 1), 88494-70-6; **95** (isomer 2), 88494-71-7; **96**, 88441-85-4; **97**, 88441-86-5; **98**, 88441-87-6; **99**, 88441-88-7; **100**, 88441-89-8; $PhCH(OEt)_2$, 774-48-1; $PhCH(OMe)_2$, 1125-88-8; p-$ClC_6H_4CH(OMe)_2$, 3395-81-1; p-$CH_3C_6H_4CH(OMe)_2$, 3395-83-3; $PhCH{=}CHCH(OMe)_2$, 4364-06-1; (E)-n-$PrCH{=}CHCH(OMe)_2$, 18318-83-7; n-$C_5H_{11}CH(OMe)_2$, 1599-47-9; n-$C_9H_{19}CH(OMe)_2$, 7779-41-1; $(C_2H_5)_2C(OMe)_2$, 25636-49-1; $EtOCO(CH_2)_2COOEt$, 123-25-1; $ClIsMe_3$, 75-77-4; PhCHO, 100-52-7; PhSCl, 931-59-9; $Ph_3CH_3P^+Br^-$, 1779-49-3; cyclohexanone dimethyl ketal, 933-40-4; cyclohexanone diethyl ketal, 1670-47-9; cyclooctanone dimethyl ketal, 25632-03-5; cyclododecanone dimethyl ketal, 950-33-4; 2-allylcyclohexanone dimethyl ketal, 88441-90-1; norbornanone dimethyl ketal, 10395-51-4; 3-methylcyclohexanone dimethyl ketal, 18349-16-1; 2-methylcyclohexanone dimethyl ketal, 38574-09-3; dihydrojasmone, 1128-08-1; 2-((methoxycarbonyl)methyl)cyclohexanone, 13672-64-5; 4-methyl-3-cyclohexenone propylene ketal, 88441-96-7; 4-hydroxy-4-(4-methyl-3-cyclohexenyl)butanoic lactone, 88441-99-0; furfural, 98-01-1.

Base-Induced Rearrangement of 1-(Trimethylsilyl)allylic Alcohols. Stereo- and Regioselective Synthesis of Silyl Enol Ethers through Lithium Homoenolates[1]

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Abstract: 1-(Trimethylsilyl)allylic alcohols have been prepared and their conversions to silyl enol ethers have been examined. Under appropriate conditions, lithium alkoxides of the above alcohols are in equilibrium with lithium homoenolates, 3-(trimethylsiloxy)allyllithiums, which react with alkyl iodides to give the silyl enol ethers of defined stereo- and regiochemistry. Further, a catalytic amount of butyllithium induces the rearrangement of the alcohols to yield the corresponding silyl enol ethers in a highly stereo- and regiocontrolled manner via self-protolysis. Equilibrium composition between lithium alkoxides and lithium homoenolates has been shown to be greatly influenced by the steric factors around α carbons of allylic alcohols.

Since the works of Stork,[2] House,[3] and then Mukaiyama,[4] silyl enol ethers have been employed as one of the most promising nucleophilic substrates in organic synthesis. Use of this class of compounds has allowed the introduction of a variety of functional groups or carbon chains onto α carbons of the carbonyl compounds.[5] Most of the procedures described for their preparation have resorted to the same basic principle: generation of enolate anions from carbonyl compounds and their silylation with an appropriate reagent. The differences of kinetically and thermodynamically favorable enolate anions have been utilized to reserve the regiochemistry of the resulting silyl enol ethers.[3] However, much difficulty has been encountered in controlling regiochemical integrities where such differences are very small or negligible, typically with ketones of similar substitution patterns such as R^1CH_2–CO–CH_2R^2 or R^1R^2CH–CO–CHR^3R^4.

In addition to regiochemistry of enolates, much attention has recently been attracted to the geometry of an enol derivative because it often has a marked influence on the stereochemical outcome of reaction products, e.g., an aldol adduct.[6] A few methods have been described so far to control the stereochemistry of silyl enol ethers,[7] but the range of their application is restricted to symmetrically substituted ketones or carbonyl compounds enolizable on only one side.

By way of well-documented 1,2-migration of the silyl group from carbon to oxygen,[8] we have explored another indirect

Table 1. Preparation of 1-(Trimethylsilyl)allylic Alcohols 4

R^1	R^2	R^3	method	yield, %
C_2H_5	H	H	A[a]	92
C_4H_9	H	H	A	96
C_6H_{13}	H	H	A	96
C_8H_{17}	H	H	A	90
$C_6H_5CH_2$	H	H	A	100
-$(CH_2)_5$-		H	A	80[b]
C_2H_5	H	CH_3	A	95
C_4H_9	H	CH_3	A	89
$C_6H_5CH_2$	H	CH_3	A	92
$C_6H_5CH_2$	H	C_4H_9	A	90
C_3H_7	CH_3	H	A	64[b]
C_2H_5	C_2H_5	H	A	58[b]
C_3H_7	CH_3	CH_3	A	80[b]
C_2H_5	C_2H_5	CH_3	A	76[b]
-$(CH_2)_5$-		C_4H_9	B[c]	93[d] × 85[e]
C_2H_5	C_2H_5	C_4H_9	B	87[d] × 92[e]

[a] Method A refers to the preparation from an acyltrimethylsilane and vinylmagnesium bromide. [b] A substantial amount of the silyl enol ether **5** was also formed in this case. [c] Method B refers to the preparation from the reaction of an acyltrimethylsilane with a magnesium acetylide followed by partial reduction. [d] Yield of the 1-(trimethylsilyl)propargyl alcohol. [e] Yield of the partial reduction of the propargyl alcohol.

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